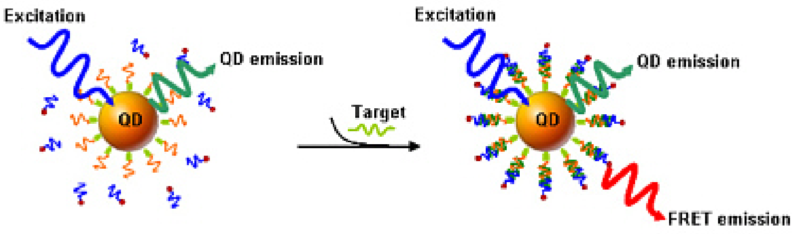
New nanosensor uses quantum dots to detect DNA

Using tiny semiconductor crystals, biological probes and a laser, Johns Hopkins University engineers have developed a new method of finding specific sequences of DNA by making them light up beneath a microscope.



DNA probes capture the target strands of DNA, then stick to a quantum dot, which is a tiny crystal of semiconductor material. When a laser shines on the quantum dot, it transfers the energy to the DNA probes, which light up through a process called fluorescence resonance energy transfer or FRET.

The researchers, who say the technique will have important uses in medical research, demonstrated its potential in their lab by detecting a sample of DNA containing a mutation linked to ovarian cancer.

The Johns Hopkins team described the new DNA nanosensor in a paper published in the November 2005 issue of the journal *Nature Materials*.

"Conventional methods of finding and identifying samples of DNA are cumbersome and time-consuming," said Jeff Tza-Huei Wang, senior author of the paper and supervisor of the research team. "This new technique is ultrasensitive, quick and relatively simple. It can be used to look for a particular part of a DNA sequence, as well as for genetic defects and mutations."

The technique involves an unusual blend of organic and inorganic components. "We are the first to demonstrate the use of quantum dots as a DNA sensor," Wang said.

Quantum dots are crystals of semiconductor material, whose sizes are only in the range of a few nanometers across. (A nanometer is one-billionth of a meter.) They are traditionally used in electronic circuitry. In recent years, however, scientists have begun to explore their use in biological projects.

Wang, an assistant professor in the Department of Mechanical Engineering and the Whitaker Biomedical Engineering Institute at Johns Hopkins, led his team in exploiting an important property of quantum dots: They can easily transfer energy. When a laser shines on a quantum dot, it can pass the energy on to a nearby molecule, which in turn emits a fluorescent glow that is visible under a microscope.

But quantum dots alone cannot find and identify DNA strands. For that, the Johns Hopkins team used two biological probes made of synthetic DNA. Each of these probes is a complement to the DNA sequence the researchers are searching for. Therefore, the probes seek out and bind to the target DNA.

Each DNA probe also has an important partner. Attached to one is a Cy5 molecule that glows when it receives energy. Attached to the second probe is a molecule called biotin. Biotin sticks to yet another molecule called streptavidin, which coats the surface of the quantum dot.

To create their nanosensor, the researchers mixed the two DNA probes, plus a quantum dot, in a lab dish containing the DNA they were trying to detect. Then nature took its course. First, the two DNA probes linked up to the target DNA strand, holding it in a sandwich-like embrace. Then the biotin on one of the probes caused the DNA "sandwich" to stick to the surface of the quantum dot.

Finally, when the researchers shined a laser on the mix, the quantum dot passed the energy on to the Cy5 molecule that was attached to the second probe. The Cy5 released this energy as a fluorescent glow. If the target DNA had not been present in the solution, the four components would not have joined together, and the distinctive glow would not have appeared. Each quantum dot can connect to up to about 60 DNA sequences, making the combined glow even brighter and easier to see.

To test the new technique, Wang's team obtained DNA samples from patients with ovarian cancer and detected DNA sequences containing a critical mutation. "This method may help us identify people at risk of developing cancer, so that treatment can begin at a very early stage," Wang said.

Source: Johns Hopkins University