Nanotechnology Highlight

Nanotechnology and a New Form of DNA

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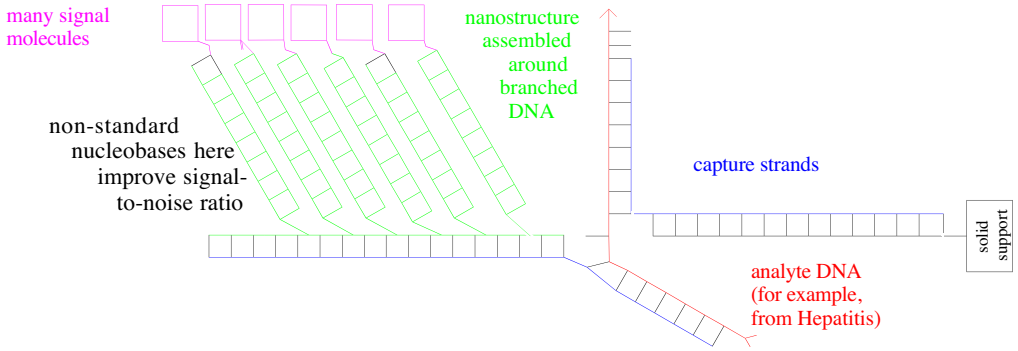
Scientists at the University of Florida have created an artificial genetic system that behaves like natural DNA, but does Nature one step better, incorporating 12 letters into the genetic "alphabet" instead of the four found in natural DNA. Scientists working at EraGen Biosciences and Chiron Corporation have grabbed this advance in fundamental science, and turned it into a molecular bonanza, supporting clinical diagnostics tools today, and possibly personalized medicine tomorrow.

DNA forms its famous "double helix" when two DNA strands come together to form a ladder-like duplex. In forming the duplex, the four "letters" of natural DNA (A, T, G, and C) pair with defined rules. A from one strand pairs preferentially with T on the other, while G on one strand pairs preferentially with C on the other. This process, known as hybridization, underlies all of genetics.

Not surprisingly, physicians very much want to detect DNA in samples taken from their patients. Unwanted DNA causes disease, from AIDS to hepatitis, and the identification of unwanted DNA is key to diagnosis of these diseases, while the amount of unwanted DNA is a key factor in determining the progress of any treatment and the prognosis for the future. Accordingly, scientists at Chiron set out to use the unwanted DNA (the red strand in the Figure) to capture onto a solid support a "nanostructure" (green), a branched DNA molecule that carried many signaling molecules (violet) that emit light. If the red DNA were present, they reasoned, the solid support would glow from the signal molecules attached to it by way of the unwanted DNA.



The problem? The nanostructure was assembled using the DNA ladders built from base pairing between A, T, G, and C, the very same letters found in natural DNA, both wanted and unwanted. There was too much of this DNA in biological tissues, and this created so much noise that the signal could not be detected unless there were more than 100,000 nucleotides in the patient sample.

Enter the Benner laboratory. Working first in Switzerland, and then at the University of Florida with support from the nanobiotechnology program from the National Science Foundation, they realized that they could create additional letters for DNA. These letters could also be designed to pair with each other, but not to pair with A, T, G, and C. When the extra letters were used to assemble the nanostructure, leaving A, T, G, and C behind to capture the unwanted DNA, the noise all but disappeared. The assay, now marketed under the brand name Quantiplex by Bayer, is one of the fastest growing new diagnostics systems available.

The artificial genetic system is now being turn on the task of identifying small changes in DNA that make individual humans different. In particular, changing a single letter in a DNA molecule creates a "single nucleotide polymorphism", called a SNP. "SNPs are often responsible for the fact that different patients react differently to therapy" notes Dr. James Prudent, who leads the team of chemists at EraGen Biosciences that is developing new diagnostics tools using Benner's artificial genetic system. "If we can detect which SNPs are present in a patient, we will soon be able to decide the best therapy to manage the patient's disease."

Prudent and his team are exploiting many unusual features of the expanded genetic alphabet to build useful tools. They envision an assay, possibly in the doctors office, that will be able to detect hundreds of SNPs at one time. This will enable "personalized medicine", to replace the "one size fits all" therapeutic regimens that characterizes contemporary medicine. "We should all benefit", he says.