Researcher creates novel 'bioelectronic signatures' to detect DNA mutations

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A new method to identify DNA mutations may shepherd in an era of small, portable, electronic devices for the rapid screening and identification of genes that harbor disease.

Joseph Wang, director of the Center for Bioelectronics and Biosensors at the Biodesign Institute at ASU, led a team that successfully merged efforts in the fields of biosensors, electronics, and nanotechnology to fashion nanocrystals that can act as "DNA biosensors" by electronically recognizing subtle mutations in the DNA. This creates enormous potential for applications such as the diagnosis and treatment of genetic diseases, detection of infectious agents and reliable forensic analysis.

Wang, who recently was recruited to the Biodesign Institute and serves a joint appointment as professor in the chemical and materials department at the Ira A. Fulton School of Engineering and Department of Chemistry at ASU, is a renowned expert in nanomaterial-based biosensors that operate at the scale of a thousand times smaller than the width of a human hair. He authored 660 papers and has 12 patents to his credit, including involvement in the development of the first noninvasive biosensor for diabetes, the FDA approved Gluco Watch, which monitors glucose levels through human sweat.

"The ultimate goal is to make something similar to a hand-held glucose monitor for future genetic testing," Wang says. "The electronic detection of DNA is a thing of beauty. You can make it small, low-power, inexpensive and robust, creating all sorts of advantages."

Among the keys to unearthing the mysteries behind individual genetic variation and diseases like cancer are fine differences – single nucleotide polymorphisms, or "SNPs" – buried within the 3 billion chemical bases of DNA comprising the human genome. Not every SNP found will necessarily cause a mutation or determine our eye or hair color – but, on average, SNPs occur about once in every 1,000 DNA bases, adding up to 3 million potential individual differences across the human genome. Wang's method allows for an accurate, ultra-sensitive, rapid and low-cost identification of these SNP variants.

"The novelty of the approach is the combination of the nanocrystal tagging of DNA to create electro-diverse signatures and combining them with a fast, portable, low-cost electronic detection," Wang says.

To achieve the desired results, Wang and his researchers custom-made several individual nanocrystals, known as quantum dots, from four heavy metal salts of lead, cadmium, zinc and copper. Such nanocrystals were selected owing to their ability to yield distinct electronic signatures, with four well-resolved current peaks. Next, the nanocrystals are piggybacked onto individual DNA bases; these DNA bases – each carrying a single nanocrystal – bind to a DNA sample and cause minute electrical current changes in the nanocrystal that can be measured with an electrode. The individual base-conjugated nanocrystals are added sequentially to any DNA sample of interest, generating an electronic "fingerprint" that rapidly identifies all possible combinations of SNPs in a single experimental run.

The whole procedure can detect SNPs in as little as two hours, which represents a vast improvement over existing laborious and time-consuming DNA detection methods. Additionally, unlike current technology, all the steps are carried out at room temperature.

The approach also is readily adaptable for identifying protein targets or single virus molecules, which is what makes it suitable for diagnosing genetic diseases, detecting infectious agents and providing reliable forensic analysis. In addition, the technology is scalable for the so-called "high throughput," or large-scale DNA sequencing efforts used by many of today's biotech companies and genomic researchers.

Though Wang is careful to admit that his results represent just the first preliminary steps for this new technology, he ultimately envisions a day when a patient can walk into a doctor's office and have their DNA checked for diseases, much like at a supermarket checkout scanner.

"The technology is evolving and we would like to extend it toward making a practical device," he says.

Wang's results recently were featured as the cover story of Analytical Chemistry and were published earlier in the Journal of the American Chemical Society. The article can be found on the Web at (pubs3.acs.org/acs/journals/doi … oi=10.1021/ja043780a). His research was supported through a grant from the National Science Foundation.

Source Arizona State University