SENSORS AND PROBES

Polymers for protein detection

Nanotube arrays, imprinted with proteins, can be used as biosensors.

Antibodies are commonly used to detect proteins, but techniques to make antibodies tend to be time-comsuming and costly. What is more, the antibodies themselves are often delicate, requiring precise conditions to retain their efficacy. Now, Dong Cai and colleagues at Boston College report a way to make robust, protein-detecting biosensors from synthetic nanomaterials.

The biosensors contain molecular imprints of the protein to be detected. To make them, the researchers began with arrays of nanotubes. They coated the tips of the tubes with a layer of nonconducting polyphenol into which they imprinted desired template proteins. Then they extracted these proteins, leaving behind holes in the polyphenol layer that closely matched the protein shape. The 'imprint holes' also decreased electrical impedance across the nanotube array. If the researchers added samples containing the protein to the array, however, these holes were filled and impedance was restored.

The team first made an array to detect human ferritin and showed that although this protein generated a signal, bovine muscle extracts and homologous horse proteins did not. Similarly, an imprint made from the human papillomavirus derived E7 protein could detect that protein at levels of picograms per liter but not the related E6 protein. The researchers next generated an array that could discriminate between conformations of calmodulin.

Cai says that, compared to antibodies, producing and using molecular imprints could be cheaper, faster and more convenient. Making an imprinted array takes about three days. Protein detection takes less than five minutes. The arrays are stable for extended periods over a wide range of conditions, and the way that proteins are incorporated into the nanoarray during imprinting can be used to fine-tune desired affinity. However, the template proteins used to imprint the array must be extremely pure to ensure specificity.

The researchers are working on ways to computationally design imprints that can guide molecular imprint fabrications for higher performance. With additional optimization, Cai believes imprinted biosensors might be used eventually in clinical diagnosis and biodefense to detect pathogens, toxins and even mutated or post-transcriptionally modified proteins.

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RESEARCH PAPERS

Cai, D. *et al.* A molecular-imprint nanosensor for ultrasensitive detection of proteins. *Nat. Nanotechnol.* advance online publication (27 June 2010).