ANALYTICAL CURRENTS

Detecting cancer markers with nanowires

Multiplexed detection of (1) PSA, (2) CEA, and (3) mucin on an array of silicon-nanowire devices functionalized with PSA-, CEA-, or mucin-specific antibodies. (Adapted with permission. Copyright 2005 Nature Publishing Group.)

Charles Lieber and colleagues at Harvard University have developed a multiplexed, label-free detection technique based on silicon-nanowire field-effect devices. With the new strategy, protein cancer markers can be reproducibly detected at femtomolar concentrations with high selectivity.

The researchers can assemble up to ~200 silicon nanowires in an array on a chip. After the device is fabricated, monoclonal antibodies (mAbs) for cancer markers are attached to the nanowires. A conductance change is observed when a cancer marker binds to an mAb on a nanowire.

To test the sensitivity of the chip, Lieber and colleagues flowed a solution containing prostate-specific antigen (PSA) onto a chip with nanowires attached to PSA mAbs. A reversible conductance change was only observed when the PSA solution was delivered.

The researchers then fabricated arrays with mAbs that were either specific for free PSA, called mAb1, or that bind to both PSA and the PSA–α1-antichymotrypsin (PSA–ACT) complex, called mAb2. When PSA was delivered, the conductance changed for both mAb1 and mAb2 nanowires. But when a PSA–ACT solution was flowed over the array, conductance changes were only observed for mAb2 nanowires.

PSA was also specifically detected in human serum and spiked donkey serum samples on arrays of mAb1 nanowires and nanowires passivated with ethanolamine. In addition, specific conductance changes were observed when PSA, carcinoembryonic antigen (CEA), or mucin solutions were successively flowed onto a chip that contained nanowires attached to mAb1 and mAbs for CEA and mucin.

Finally, Lieber and colleagues detected the activity of telomerase, a suspected cancer marker, on nanowire chips. They attached DNA strands with telomerase binding sites to nanowires. The addition of HeLa cell extracts containing telomerase caused a conductance change. The addition of nucleotides to the chip caused another conductance change, which indicates that the telomerase enzyme incorporated the nucleotides into the DNA strand. (*Nat. Biotechnol.* **2005**, *23*, 1294–1301)

Turning aptamers into sensors

Kevin Weeks and Edward Merino at the University of North Carolina at Chapel Hill have developed a simple method for converting aptamers into sensors. The investigators say their approach of creating 2′-ribose-derivatized aptamers provides a way to create rationally designed, reagentless sensors for small molecules.

The new technique allows existing aptamers to be fluorescently labeled without prior knowledge of their structures. Weeks and Merino attached the Bodipy-FL fluorophore to DNA aptamers that recognized adenosine monophosphate (AMP), argininamide, and tyrosinamide. A series of fluorescent adducts of the three aptamers was synthesized and tested for ligand specificity. From the series, 5 effective ligand-sensing adducts showed >40% change in fluorescence intensity upon binding their ligands.

The investigators also tested the aptamer adducts as reagentless sensors under biologically realistic conditions. They used 50% (v/v) unmanipulated human urine and 25% (v/v) fetal bovine serum solutions as test cases. The solutions provided challenging environments because they exhibit considerable background fluorescence and contain high concentrations of salt. The AMP and tyrosinamide sensors functioned well under these conditions, exhibiting binding affinities identical to those in buffer. The argininamide sensor didn't bind its ligand under the test conditions, however, because the aptamer was originally selected to function at low NaCl concentrations. (*J. Am. Chem. Soc.* **2005**, *127*, 12,766–12,767)