# New approaches and applications of nanostructured microfluidic immunoarrays for cancer biomarker proteins

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Sensitive measurement of biomarker proteins overexpressed in individuals with cancer holds great promise for early cancer detection and personalized therapies. Broad implementation of such diagnostic strategies requires reliable, inexpensive devices to measure multiple proteins in patient samples. Emerging aspects of nanotechnology provide exciting new opportunities to design and fabricate such devices. In this paper, we technical advances for the ultrasensitive multiplexed detection of proteins in patient serum and tissue lysates samples. These approaches are based first on nanostructured sensor surfaces to achieve high levels of capture antibodies in efficient conformations, and novel labeling strategies that achieve very large signal amplification. Microfluidic immunoarrays utilizing amperometry interfaced with microfluidics achieved well-controlled mass transport leading to excellent signal/noise and unprecedented sensitivities. The 8-electrode array chips are gold arrays fabricated by ink-jet printing of 4 nm alkylthiol gold nanoparticles, or commercial screen printed carbon coated with 5 nm glutathione-gold nanoparticles. The gold arrays are printed on heat treatable plastic sheets and insulated by over-printing a polymer layer, then annealed. The gold sensor elements are coated with self-assembled monolayers providing functionality to attach capture antibodies to their surfaces. These arrays are fitted into a PDMS microfludic channel attached to a syringe pump and injector to deliver reagents and samples. Multilabel approaches include massively enzyme-labeled magnetic particles used with an on-line analyte capture chamber in the device. These approaches greatly amplify the signals for analyte proteins, and detection limits as low as 5 fg $mL^{-1}$ have been achieved for multiple proteins in serum using assays taking about 1.1 hr. Applications to biomarker proteins for oral cancer, metastasis, and inflammation will be discussed. For detection of metastatic biomarkers during surgery, high sensitivity can be traded for speed to achieve immunoassays in less than 10 min.