Ultrasensitive Detection of Cancer Biomarkers in the Clinic by Use of a Nanostructured Microfluidic Array

Type: Article

Abstract:
Multiplexed biomarker protein detection holds unrealized promise for clinical cancer diagnostics due to lack of suitable measurement devices and lack of rigorously validated protein panels. Here we report an ultrasensitive electrochemical microfluidic array optimized to measure a four-protein panel of biomarker proteins, and we validate the protein panel for accurate oral cancer diagnostics. Unprecedented ultralow detection into the 5-50 fg.mL(-1) range was achieved for simultaneous measurement of proteins interleukin 6 (IL-6), IL-8, vascular endothelial growth factor (VEGF), and VEGF-C in diluted serum. The immunoarray achieves high sensitivity in 50 min assays by using off-line protein capture by magnetic beads carrying 400 000 enzyme labels and similar to 100 000 antibodies. After capture of the proteins and washing to inhibit nonspecific binding, the beads are magnetically separated and injected into the array for selective capture by antibodies on eight nanostructured sensors. Good correlations with enzyme-linked immunosorbent assays (ELISA) for protein determinations in conditioned cancer cell media confirmed the accuracy of this approach. Normalized means of the four protein levels in 78 oral cancer patient serum samples and 49 controls gave clinical sensitivity of 89% and specificity of 98% for oral cancer detection, demonstrating high diagnostic utility. The low-cost, easily fabricated immunoarray provides a rapid Serum test for diagnosis and personalized therapy of oral cancer. The device is readily adaptable to clinical diagnostics of other cancers.

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