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Optomechanical devices for Deep Plasma Cancer Proteomics

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Most of the cancer deaths could be avoided by early detection of the tumor when it is confined to its primary site and it has not metastasized. To this aim, one of the most promising strategies is the discovery and detection of protein biomarkers shed by the young tumor to the bloodstream. Proteomic technologies, mainly mass spectrometry and multiplexed immunoassays, have rapidly developed during last years with improved limits of detection and multiplexing capability. Unfortunately, these developments together major investments and large international efforts have not resulted into new useful protein biomarkers. Here, we analyze the potential and limitations of current proteomic technologies for detecting protein biomarkers released into circulation by the tumor. We find that these technologies can hardly probe the deepest region of the plasma proteome, at concentrations below the pg/mL level, where protein biomarkers for early cancer detection may exist. This clearly indicates the need of incorporating novel ultrasensitive techniques to the proteomic tool-box that can cover the inaccessible regions of the plasma proteome. We here propose biological detectors based on nanomechanical systems for discovery and detection of cancer protein biomarkers in plasma. We review the modes of operation of these devices, putting our focus on recent developments on nanomechanical sandwich immunoassays and nanomechanical spectrometry. The first technique enables reproducible immunodetection of proteins at concentrations well below the pg/mL level, with a limit of detection on the verge of 10 ag/mL. This technology can potentially detect low abundance tumor-associated proteins in plasma at the very early stages of the tumor. The second technique enables the identification of individual intact proteins by two physical coordinates, the mass and stiffness, instead of the mass-to-charge ratio of the protein constituents. This technology enormously simplifies the identification of proteins and it can provide useful information on interactions and posttranslational modifications, that otherwise is lost in mass spectrometry.

Keywords

Early cancer detection, cancer biomarkers, human proteomics, plasma proteomics, mass spectrometry, immunodetection, antibody arrays, nanomechanical systems, ultrasensitive biosensors, nanomechanical spectrometry