Hybrid optoplasmonic and nanomechanical sensor for proteomics

Priscila M. Kosaka
Sergio Garcia, Montserrat Calleja & Javier Tamayo

Instituto de Micro y Nanotecnología (IMN-CNM), CSIC, Tres Cantos, Madrid, Spain

p.m.kosaka@csic.es

Blood contains an unknown treasure trove of protein biomarkers that will be crucial for early detection of cancer or other fatal diseases and for personalized medicine. Current proteomic technologies have developed rapidly during recent 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. A fundamental reason for this dismal progress is the extraordinary complexity of the human plasma that comprises more than 10,000 protein species with known concentrations ranging more than 10 orders of magnitude. It is expected that biomarkers for early cancer or infectious disease detection are at concentrations of at least one million times lower than blood proteins, which is well-below the bottom of the current detection limits in proteomics. Although, the analytical capability of proteomic technologies is rapidly improving, there is an urgent need of new ultrasensitive technologies that can access to the deepest part of the human plasma proteome[1].

In this talk I will present a hybrid nanomechanical and optoplasmonic nanosensor we have developed recently. The immunoassay comprises a sandwich assay that involves the recognition of a protein biomarker first by a surface-anchored antibody and second by an antibody free in solution that recognizes a free region of the captured biomarker. This second antibody is tethered to a gold nanoparticle that acts as mass and plasmonic label. The double signature is detected by means of a silicon cantilever that serves as mechanical resonator for 'weighing' the mass of the captured nanoparticles; and as optical cavity due to the two reflective opposite surfaces, that boosts the plasmonic signal from the nanoparticles. Merging mechanical and optical transduction schemes in the same platform provides remarkably superior performance and higher reliability than devices based on a single transduction scheme. The concept was demonstrated with two cancer biomarkers, the carcinoembryonic antigen (CEA) and the prostate specific antigen (PSA). An unprecedented detection limit of 1×10^{-16} g ml^{-1} in serum was achieved with both biomarkers[2], which is at least seven orders of magnitude better than that achieved in routine clinical practice. Very recently the hybrid nanosensor was also challenged for the early detection of HIV-1 in human serum [3]. Again, the limit of detection achieved was of 10×10^{-16} g ml^{-1}, which is equivalent to only one virus in 10 mL of blood. More importantly, the immunoassay confidence is of 95%. Due to the ultrasensitivity of our nanosensor the undetectable phase after HIV infection could be reduced to just one week and the dreamed early detection of cancer could be a reality in the future. Moreover, the presented hybrid sensor is simple and affordable, and thus it can be easily implemented in health systems.

References

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