Title: Nanoparticle-enhanced surface plasmon resonance imaging for advanced clinical diagnostics

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A major challenge in the area of DNA biosensors is the development of rapid and multiplexed methods that do not require the labeling and the polymerase chain reaction amplification of the genetic samples. Both the above steps increase the cost and the complexity of the assay. In this perspective, our strategy based on the combined use of Surface Plasmon Resonance Imaging (SPRI), Peptide Nucleic Acid (PNA) probes and bioconjugated gold nanoparticles (AuNPs) has been shown to produce an ultrasensitive detection of nucleic acids which could lead to more reliable and sensitive diagnostics assays. The detection of the target sequence was achieved by adopting a sandwich hybridization strategy using AuNPs conjugated to an oligonucleotide complementary to the final tract of the DNA target, which is not involved in the hybridization with the SPRI sensor surface-immobilized PNA probe. This strategy allowed discrimination between fully matched and single base-mismatched sequences with a sensitivity down to femtomolar range. The reduced number of genomic DNA equivalents required for the analysis allows us to propose the method we describe as a potential new tool for the analysis of rare cell populations, such as DNA and RNA biomarkers freely circulating in the blood as liquid biopsy. Such methods are expected to provide new opportunities for a better understanding of cancer disease at the molecular level, thus contributing to improved patient outcomes.