

Ultraflat, Ultraclean Au Nanoplate for Supersensitive Detection of Anti-CCPs

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Extended Abstract

Gold is very stable in biochemical environments and can immobilize easily bioactive molecules including DNAs, aptamers, antibodies, and peptides through Au-S bonding. In addition, gold is an excellent plasmonic material and has been widely used for fabrication of sensitive sensors. However, intrinsic surface defects of gold, such as step, terrace, vacancy, and grain boundary, are major problems for perfect immobilization of the biochemical molecules.[1] So, top-down polishing including thermal annealing, UV-ozone cleaning, and hydroxyl radical etching has been employed to reduce the surface defects, but being hardly possible to eliminate them completely.[2] On the other hand, Au nanoplates synthesized in vapor phase have atomically smooth surfaces without any surface defects, being able to construct a highly well-ordered bio-molecular layer from coherently linked metal-molecule interface.

Highly-selective detection of anti-cyclic citrullinated peptides (anti-CCPs) has been an important issue to diagnose early rheumatoid arthritis (RA). Anti-CCP is a highly specific biomarker (90%-95%) for RA, being in a very small quantity at early RA which does not show clinical symptoms.[3] Since it takes several months or even years to be characterized as RA from the chronic inflammation occurred at the synovial joints, the sensitivity is more important than detection time to identify the RA patients in early-stage. However, current sensors based on enzyme-linked immunosorbent assay (ELISA) methods have been focused on rapid detection of anti-CCPs. Recently, Dubacheva et al. reported super-selective targeting employing a well-defined self-assembled monolayer (SAM) formed on UV-ozone treated gold surface.[4] Because non-specific binding can cause false-positive signals and increase the zero-signal intensity, it is a key-factor which reduces the sensor's sensitivity. Therefore, super-selective detection of the anti-CCPs by a well-defined CCP layer would play an important role in diagnosis of early RA.

Surface-Enhanced Raman Scattering (SERS) sensors employing hot spots by nanoscale gap between noble metal nanostructures have been much attention because of single molecule level sensitivity.[5] Here, we report that anti-CCP SERS sensor fabricated with ultraflat, ultraclean, and single-crystalline Au nanoplate can detect even 40 aM (0.1 pg/ml) of anti-CCPs due to highly reduced nonspecific bindings as 50 times compared to commercial Au film. The well-ordered CCPs on Au nanoplates can clearly increase target signals and decrease zero-signals, being able to improve the sensitivity as 100 times than current SERS sensor. Furthermore, atomic force microscopy (AFM) studies in dry ambient environment show distinctly the super-sensitive CCP- active surfaces formed on the Au nanoplate. Thus, we expect that ultraflat Au nanoplate SERS sensors enable attomolar detection of anti-CCPs and will be utilized excellently for early-diagnosis of RA.

References

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