(SD2023-036) Matrix-insensitive approach for protease detection

Tech ID: 33216 / UC Case 2021-Z08-1

ABSTRACT

Researchers at UC San Diego have developed a dipeptide composed of two arginine (Arg-Arg) that is capable of inducing the assembly of citrate-capped gold nanoparticles (AuNPs-citrate). Surprisingly, the resulting Arg-Arg-AuNPs are stable over time as the peptide protects the particles from degradation. The assemblies can even be dried without any loss of particles. The assembly of AuNPs-citrate changes their optical properties and the color of the suspension turns from red to blue. Importantly, the assemblies can be dissociated with thiolated polyethylene glycol (HS-PEGs) molecules which leads to the recovery of the initial optical properties of the AuNPs, i.e. the red color of the suspension. Surprisingly, we have observed that such dissociation of AuNPs assemblies is not sensitive to the composition of the medium. It can thus be performed in biological fluids such as pure plasma, saliva, urine, bile, cell lysates or even sea water.

TECHNOLOGY DESCRIPTION

The detection of protease biomarker is performed by the conjugation of a peptide substrate to a HS-PEGs molecule. The resulting HS-PEG-peptide conjugate is either too bulky or too charged to dissociated the AuNPs assemblies. However, in the presence of the target protease, this latter cleaves the HS-PEG-peptide conjugate and there is a release of HS-PEGs fragment that can dissociate the assemblies and there is an unambiguous color change. The dissociation is complete after 30 minutes and the color change can be observed after only 5 minutes. This can be performed in any biological fluid and can be adapted to any protease as far as it is possible to find a peptide substrate.

This is particularly interesting because most of the nanoparticles-based sensing platforms suffer from the capacity to operate in biological fluids due to background signal caused by endogenous molecules. Finally, we have demonstrated how the assemblies dissociation with HS-PEGs can be exploited for biomarker sensing. We have shown that it is possible to conjugate, i.e. link, a peptide substrate to HS-PEGs molecules, making the resulting conjugate (HS-PEG-peptide) specific to a target protease. The presence of the protease is thus detected via the proteolytic cleavage that releases HS-PEGs fragments, inducing the dissociation of the assemblies. In the absence of proteases, the HS-PEG-peptide can not dissociate the assemblies. We showed in the manuscript the detection of a model protease, trypsin, but we also obtained results concerning the detection of the main protease of the virus SARS-CoV-2 (Mpro) in saliva.

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OTHER INFORMATION

KEYWORDS

PEG, colorimetric detection, gold nanoparticles, peptides, protease sensing, reversible assembly

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Materials & Chemicals**
  - Nanomaterials
- **Medical**
  - Diagnostics

RELATED CASES

2021-Z08-1

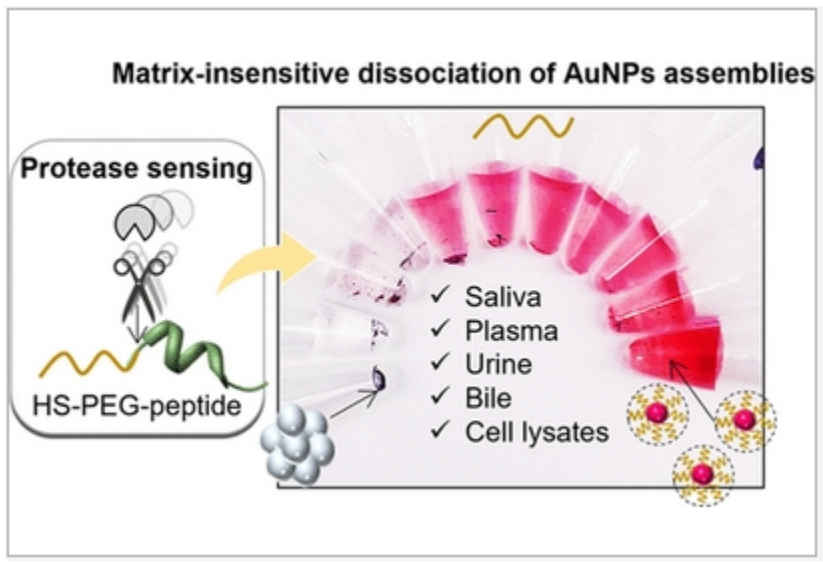
APPLICATIONS

Sensing kit for protease without the need of sample dilution or analyte extraction from the biological fluids.

For example, able to detect the main protease of SARS-CoV-2 virus in biological fluid.

ADVANTAGES

STATE OF DEVELOPMENT



INTELLECTUAL PROPERTY INFO

UC San Diego has filed for patent protection. This technology is available for commercial development.

RELATED MATERIALS

- Retout M, Jin Z, Tsujimoto J, Mantri Y, Borum R, Creyer MN, Yim W, He T, Chang YC, Jokerst JV. Di-Arginine Additives for Dissociation of Gold Nanoparticle Aggregates: A Matrix-Insensitive Approach with Applications in Protease Detection. ACS Appl Mater Interfaces. 2022 Nov 23;14(46):52553-52565. doi: 10.1021/acsami.2c17531. Epub 2022 Nov 8 - 11/08/2022

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