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Ultra-sensitive Detection of Alzheimer's Disease Protein Biomarkers Using Magnetic Nanoparticles

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ABSTRACT

Alzheimer's disease (AD) is the most prevalent cause of dementia, and detection of biomarkers such as t-tau, phospho-tau and beta-amyloid, represents an emerging method for AD screening since the expression profile of biomarkers can vary from the normal range at around 15-20 years before any dementia symptoms. We develop a direct and ultrasensitive assay based on immunoreaction between the target and corresponding antibody followed by protein turn-on fluorophore labelling to detect these protein biomarkers for AD in body fluids. Herein, we improve the detection sensitivity of the assay mentioned above by reducing the non-specific background level by introducing AuNPs as fluorescence quenchers. Lower limit of detection and higher sensitivity can be achieved which holds great promise for the early diagnosis of AD.

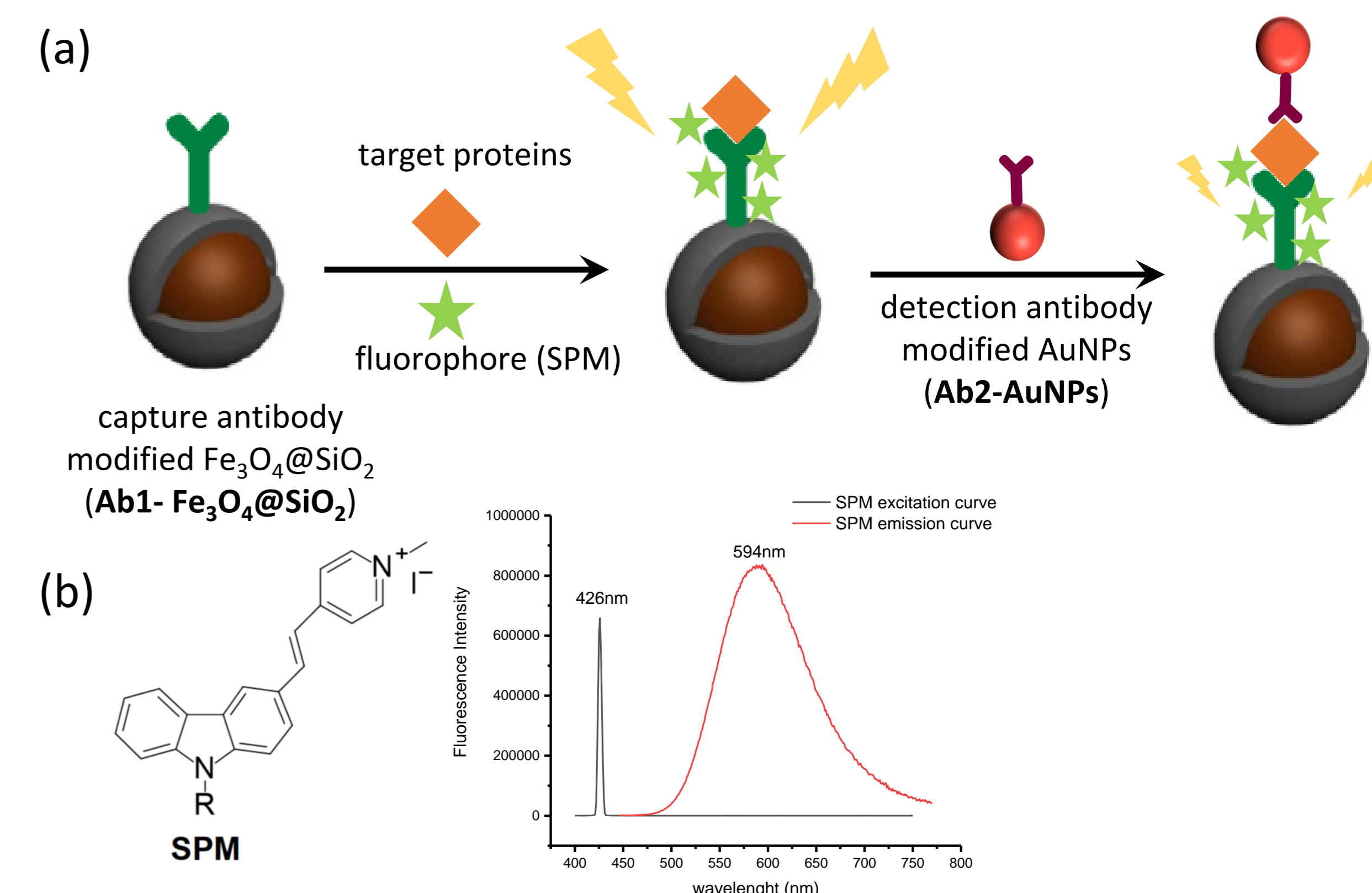
ILLUSTRATION

Figure 1. (a) Schematic illustration of the detection assay using detection antibody modified AuNPs. (b) Structure and spectrum of SPM

RESULTS

Characterization of silica coated iron oxide nanoparticles and modified AuNPs

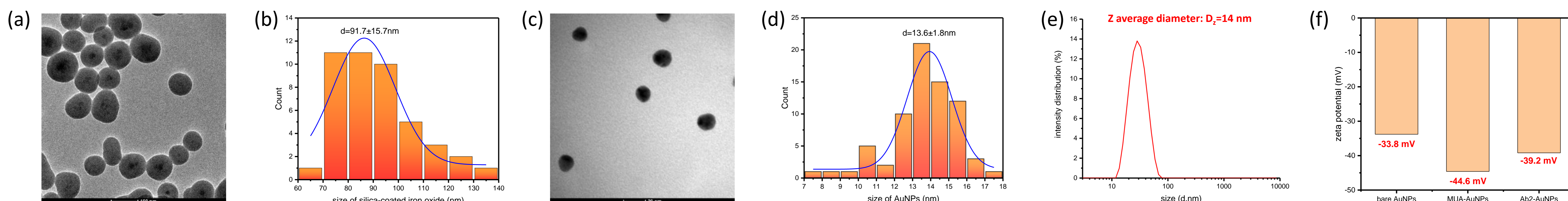


Figure 2. (a) , (b) TEM images and size distribution of silica-coated iron-oxide nanoparticles. (c) , (d) TEM images and size distribution of AuNPs. (e) Hydrodynamic diameter of bare AuNPs. (f) Zeta potential of bare AuNPs, MUA-AuNPs and Ab2-AuNPs.

RESULTS

Detection of t-tau with different procedures

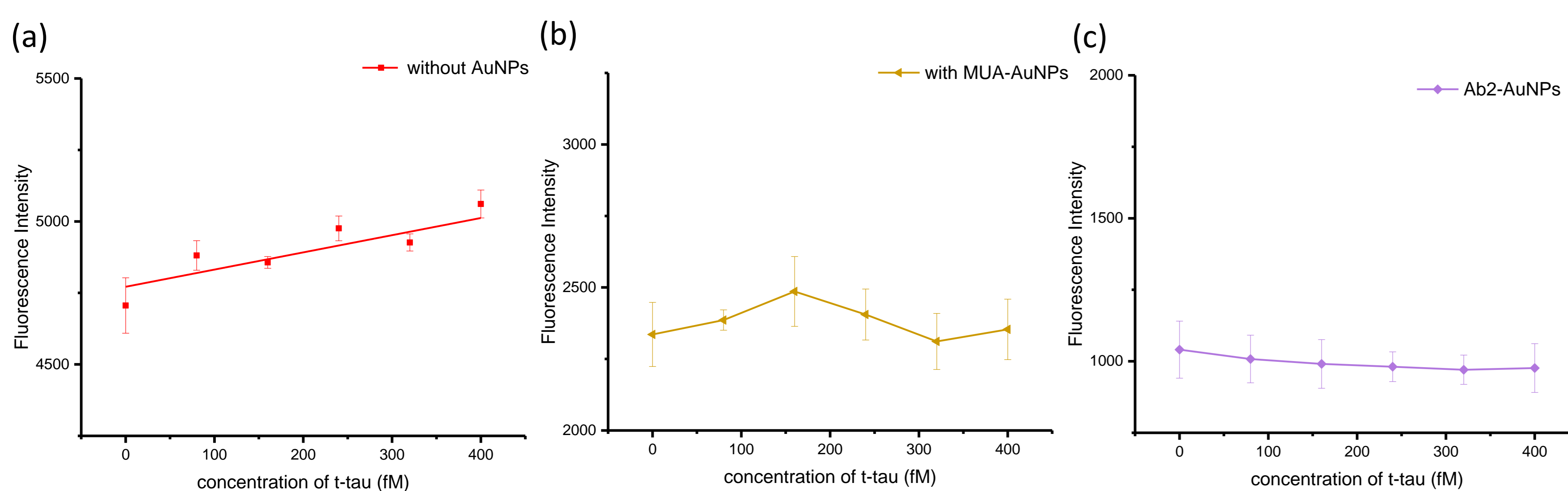


Figure 3. (a) Detection of t-tau without AuNPs. (b) Detection of t-tau with MUA-AuNPs for non-specific quenching. (c) Detection of t-tau with Ab2-AuNPs for specific quenching.

- When detecting without AuNPs, fluorescence intensity slightly increased with the increasing concentration of t-tau in low concentration range of 0-400 femtomolar and the linearity is not so good. (Figure 3. (a))
- When detecting with MUA modified AuNPs (MUA-AuNPs), fluorescence intensity was quenched but the quenching efficiency didn't show obviously target protein concentration dependency. (Fig. 3(b))
- When detecting with the detection antibody modified AuNPs (Ab2-AuNPs), fluorescence intensity was significantly quenched and slightly decreased with the increasing t-tau concentration, but the linearity and sensitivity need to be improved by optimization.

CONCLUSION

- Capture antibody modified magnetic nanoprobe and detection antibody modified AuNPs were successfully prepared.
- Detection antibody modified AuNPs can significantly quench the fluorescence, which demonstrates that they have the potential to decrease the high fluorescence from the capture antibody and to improve the sensitivity of the detection assay.

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