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Ultrasensitive photoelectrochemical immunoassay for CA19-9 detection based on CdSe@ZnS quantum dots sensitized TiO_2NWs/Au hybrid structure amplified by quenching effect of $Ab_2@V^{2+}$ conjugates

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ABSTRACT

A novel, enhanced photoelectrochemical immunoassay was established for sensitive and specific detection of carbohydrate antigen 19-9 (CA19-9, Ag). In this protocol, TiO_2 nanowires (TiO_2NWs) were first decorated with Au nanoparticles to form TiO_2NWs/Au hybrid structure, and then coated with CdSe@ZnS quantum dots (QDs) via the layer-by-layer method, producing TiO_2NWs/Au/CdSe@ZnS sensitized structure, which was employed as the photoelectrochemical matrix to immobilize capture CA19-9 antibodies (Ab_1); whereas, bipyridinium (V^{2+}) molecules were labeled on signal CA19-9 antibodies (Ab_2) to form $Ab_2@V^{2+}$ conjugates, which were used as signal amplification elements. The TiO_2NWs/Au/CdSe@ZnS sensitized structure could adequately absorb light energy and dramatically depress electron–hole recombination, resulting in evidently enhanced photocurrent intensity of the immunosensing electrode. While target Ag were detected, the $Ab_2@V^{2+}$ conjugates could significantly decrease the photocurrent detection signal because of strong electron-withdrawing property of V^{2+} coupled with evident steric hindrance of Ab_2. Thanks to synergy effect of TiO_2NWs/Au/CdSe@ZnS sensitized structure and quenching effect of $Ab_2@V^{2+}$ conjugates, the well-established photoelectrochemical immunoassay exhibited a low detection limit of 0.0039 U/mL with a wide linear range from 0.01 U/mL to 200 U/mL for target Ag detection. This proposed photoelectrochemical protocol also showed good reproducibility, specificity and stability, and might be applied to detect other important biomarkers.

1. Introduction

Sensitive and accurate detection of disease-related targets is critical to many areas of life and medical sciences, from food safety, environmental monitoring to clinical diagnosis. Especially, highly sensitive detection of cancer biomarkers shows great promise for early diagnosis and disease monitoring (Kitano, 2002; Srinivas et al., 2001). Carbohydrate antigen 19-9 (CA19-9), a Lewis antigen of the cell surface associated mucin 1 (MUC1) protein with an average molecular weight of 1000 kDa, is a gold standard for pancreatic cancer diagnosis (Gui et al., 2013; Gold et al., 2006). Elevated levels of CA19-9 also are associated with gastric, urothelial, and colorectal carcinomas (Xiao et al., 2014; Jha et al., 2013; Narita et al., 2014). Thus, sensitive detection of CA19-9 is of great importance in early prediction for related cancers and diseases. To date, a variety of methods have been developed for CA19-9 detection, such as enzyme-linked immunoassay (Heidari et al., 2014), photoluminescence (Gu et al., 2011), chemiluminescence immunoassay (Shi et al., 2014; Lin and Ju, 2005), and electrochemical immunoassay (Tang et al., 2013; Yang et al., 2015). Despite many advances of these assays, some of them have drawbacks such as evident sample volume, complicated equipment, limited sensitivity, difficult automation and high cost. Thus, development of highly sensitive, simple and inexpensive techniques for CA19-9 detection is very desirable.

Photoelectrochemical analysis is a newly emerged yet dynamically developing technique for the detection of various biological molecules. Recently, it has aroused a great research interest because of the features of simple devices, low cost and easy miniaturization than optical methods such as chemiluminescence

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