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Abstract:

A simple-prepare, single-use and cost-effective, *in vitro* biosensor for the detection of TAR DNA-binding protein 43 (TDP-43), a biomarker of neuro-degenerative disorders, was designed, manufactured and tested. This study reports the first biosensor application for the detection of TDP-43 using a novel biosensor fabrication methodology. Bioconjugation mechanism was applied by conjugating anti-TDP 43 with N-succinimidyl S-acetylthioacetate (SATA) producing a thiol-linked anti-TDP 43, which was used to directly link with gold electrode surface, minimizing the preparation steps for biosensor fabrication and simplifying the biosensor surface. The effectiveness of this bioconjugation mechanism was evaluated and confirmed by FqRRM12 protein, using nuclear magnetic resonance (NMR). The surface coverage of the electrode was analyzed by Time-of-Flight-Secondary Ion Mass Spectrometry (TOF-SIMS). Differential pulse voltammetry (DPV) was acted as the detection transduction mechanism with the use of $[\text{Fe}(\text{CN})_6]^{3-/4-}$ redox probe. Human TDP-43 peptide of 0.0005 $\mu\text{g/mL}$ to 2 $\mu\text{g/mL}$ in undiluted human serum was analyzed using this TDP-43 biosensor. Interference study of the TDP-43 biosensor using β -amyloid 42 protein and T-tau protein confirmed the specificity this TDP-43 biosensor. This bioconjugation chemistry based approach for biosensor fabrication circumvents tedious gold surface modification and functionalization while enabling specific detection of TDP-43 in less than 1hr with a low fabrication cost of a single biosensor less than \$3.

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