Electronic Supplementary Material (ESI) for Analyst.

Label-free detection of Cu (II) in human serum sample by prion proteins-immobilized FET sensors

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Stable incubation of prion-Cu^{2+} ions for sensor based on FET devices

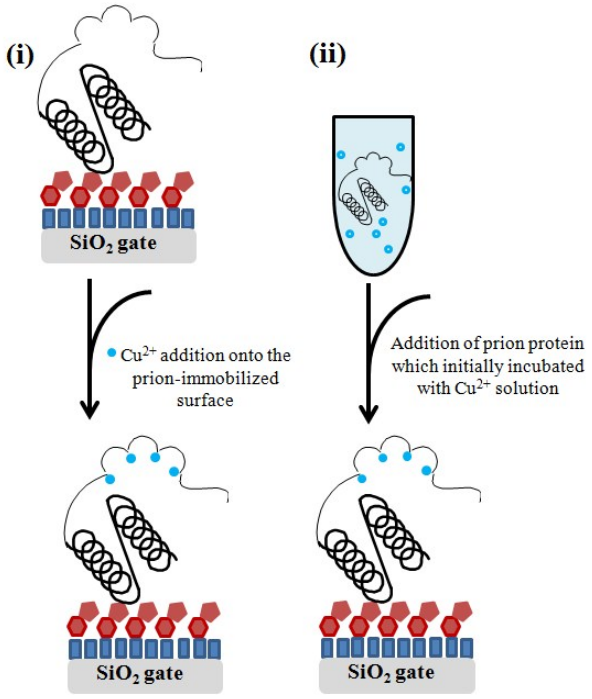

Figure S1. Schematic illustration of procedure for the addition of Cu^{2+} into the prion proteins

We examined two approaches for preparing the prion-Cu^{2+} interaction onto the FET gate surface as illustrated in Figure S1. The first procedure, after preparation of prion proteins adsorbed on the thiamine-immobilized gate surface using 40 nM prion sample, then the 100 mM Cu^{2+} solution was dipped for 10 min at room temperature onto the gate electrode (Fig. S1.i). And the second procedure (Fig. S1.ii), a sample solution containing 100 mM Cu^{2+} solution and 40 nM prion proteins in buffer was incubated in 4 ˚C during 1 h. Then the sample was dipped for 1 h at room temperature onto the thiamine-immobilized FET. After each incubation and addition of metal ion, the device was washed with 10 mM and 0.1 mM PBS for three times to reduce any non-specific adsorption.

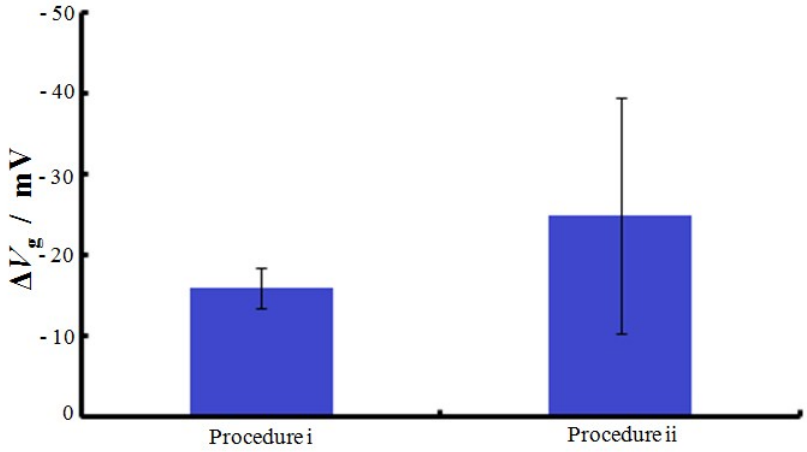

Figure S2. FET responses depended on the procedure for preparing the prion-Cu^{2+} complex

In case of the first procedure, the ΔV_g can be generated around -16 mV for three times measurements with standard deviation equal to 15,7 %. This FET response was lower than the signal caused by the second procedure in which the ΔV_g was -25 mV. It is suggested due to the efficiency of prion-Cu^{2+} interaction in particular for prion protein oligomer where some proteins attached each other as aggregates. The first procedure with reaction time of 10 min was not adequate for penetrating and interacting to all proteins adsorbed on the surface. Whereas, the second procedure can provide more efficient route for Cu^{2+} ions to be reacted with the prion proteins. However, the standard deviation for three time measurements of the second procedure was very large equal to 58,3 %. This disadvantage was suggested caused by the repulsion among Prion-Cu^{2+} complexs in solution that leads heterogeneous distribution of protein adsorbed on the thiamine-immobilized surface. To provide a reliable and stable detection, we chose the first procedure to be used in the forward experiment for further optimization.

XPS characterization for confirming the presence of copper element

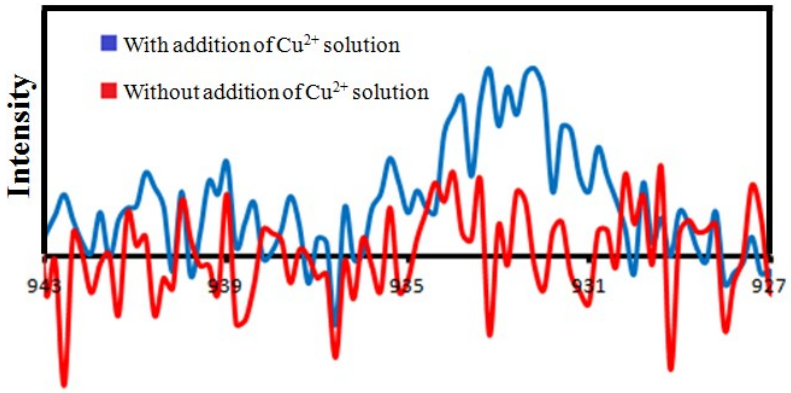

Figure S2. Narrow XPS spectra on region of Cu $2p_{3/2}$ peak

To prove the attachment of Cu^{2+} on the prion immobilized FET gate surface, XPS measurement was carried out using a spectrophotometer (Al K□ X-ray source, PHI-5000 versa probe WS, ULVAC-PHI Inc.). We examined and compared the specimens of prion immobilized thiamine surface treated with or without addition of Cu^{2+} solution. As shown in Figure S2, the Cu $2p_{3/2}$ peak at binding energy around 933 eV can be confirmed for the specimen treated with Cu^{2+} solution. This result is evidence the existence of copper species captured by prion on the surface. On the other hand, the narrow spectra was almost flat and no peak, indicating that the observed Cu peak was really occurred due to interaction of Cu with prion on the surface.

Optimization the time of reaction

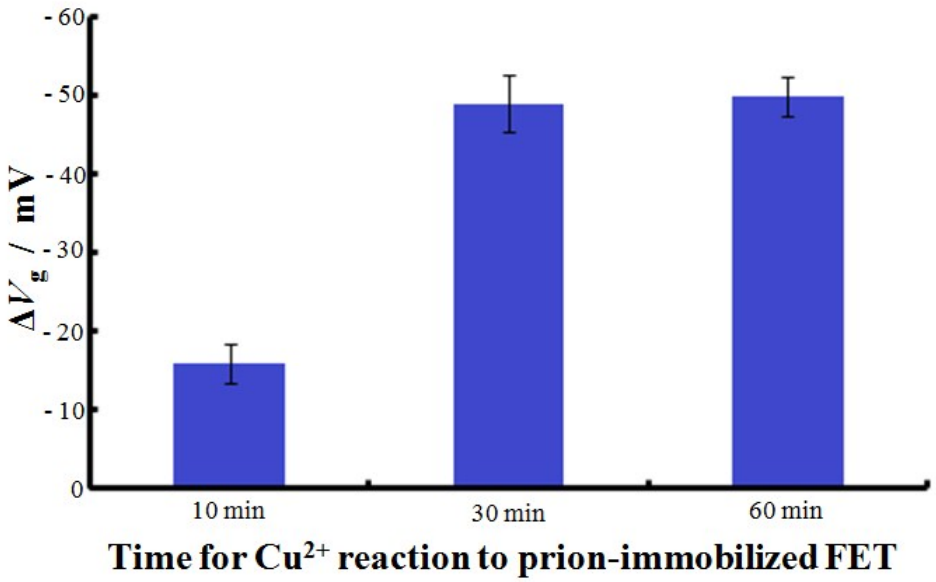

Figure S3. FET responses for Cu^{2+} detection dependence on the reaction time

Reaction time is one of the important parameter to optimize the interaction between two or more molecules. Here, examination was carried out to test the effect of reaction time for 30 min and 1 h by using 100 mM Cu^{2+} to the prion adsorbed on the gate surface (prion sample for addition onto the gate surface was 40 nM). As shown in Fig. S3, the FET signal for Cu^{2+} detection is higher for 30 min than 10 min, then the FET signal of reaction time for 1 h showed no further enhancement and quite similar with the signal on 30 min. The result suggested that the 30 min of reaction time was adequate for more penetration, diffusion and interaction of Cu^{2+} ions to the more proteins adsorbed on the surface, especially in case of oligomeric form in which the proteins aggregates each others. All experiments for the data in manuscript used 30 min as the optimal reaction time.