Electronic Supplementary Information

Three-dimensional CoNi-MOF nanosheet array-based immunosensor for sensitive monitoring of human chorionic gonadotropin with core-shell ZnNi-MOF@Nile blue nanotags

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Experimental section

Chemicals and reagents

Nickel nitrate hexahydrate ($Ni(NO_3)_2 \cdot 6H_2O$, AR) and cobalt nitrate hexahydrate ($Co(NO_3)_2 \cdot 6H_2O$, AR) are purchased from Tianjin Kermel Chemical Reagent Co., Ltd. Ethanol absolute is purchased from Tianjin Fengchuan Chemical Reagent Technology Co., Ltd. Beta-Human chorionic gonadotropin (HCG) and anti-HCG (Ab_1 and Ab_2) are brought from Shanghai Linc-Bio Science Co., Ltd. 3,5-diaminobenzoic acid, 1,4-benzenedicarboxylic acid and bovine serum albumin (BSA) are brought from Shanghai Aladdin Bio-Chem Technology Co., Ltd. Nile Blue A is purchased from Adamas Reagent, Ltd. The remaining chemicals are of analytical grade and can be used directly. Human blood samples are kindly provided by the Shuozhou Modern Hospital (Gubei Street, Shuocheng District, Shuozhou, Shanxi, China). The human serum is separated from the blood samples by centrifugation. All experiments are performed in accordance with the Guidelines “The administrative measures for clinical laboratories of medical institutions (No. 73, Rev. 2006) issued by the Department of Medical Services Supervision of the Ministry of Health of the People's Republic of China", and approved by the ethics committee at Shanxi Normal University.

Apparatus

The phase structures are analyzed by X-ray diffraction (XRD, Ultima IV-185,

Rigaku Co., Japan). The morphology and internal structure of the samples are observed by scanning electron microscopy (SEM, JEM-7500F) and transmission electron microscopy (TEM, JEM-2100). X-ray photoelectron spectrum (XPS) is acquired to determine the chemical compositions and valence states at a K-Alpha XPS spectrometer (Thermo Scientific, USA). Fourier transform infrared spectroscopy (FT-IR) spectrum is collected using FTIR-650 Fourier Transform Infrared Spectrometer (Tianjin Gangdong Sci.&Tech. Development Co., Ltd, Tianjin, China). Square wave voltammetry (SWV) electrochemical measurement is carried out on CHI660E electrochemical workstation (Chenhua Instrument Shanghai Co., Ltd., China).

Synthesis of Co-Ni layered double hydroxide nanosheet arrays

Before the preparation, the Ni foam is ultrasonically cleaned with HCl, ethanol and ultrapure water for 30 min, respectively. In a three-electrode system, electrodeposition is accomplished at room temperature. A cleaned Ni foam (1 cm × 2 cm) is used as the working electrode, Ag|AgCl electrodes and Pt foil are used as the reference electrode and the counter electrode, respectively. The electrolyte for electrochemical deposition of Co-Ni layered double hydroxides (LDHs) arrays consisted of 0.02 M of $Ni(NO_3)_2 \cdot 6H_2O$ and 0.02 M of $Co(NO_3)_2 \cdot 6H_2O$. The deposition is maintained at a constant potential of -1.0 V for 600 s. Finally, the Co-Ni LDHs arrays are rinsed with double-distilled water several times and dried at 70 °C about 9 h. Correspondingly, $Co(OH)_2$ and $Ni(OH)_2$ nanosheets array on Ni foam are also synthesized under the same experimental conditions.

Synthesis of CoNi-MOFs nanosheet arrays

Typically, 15 mg of 3,5-diaminobenzoic acid is dissolved in 4 mL of ultrapure water and 4 mL of ethanol absolute. The above solution is transferred to the Teflon liner of an autoclave. Then, Co-Ni LDHs nanosheets/Ni foam (1 cm × 2 cm) are soaked in the above reaction solution. The autoclave is sealed and heated rapidly at 140°C for 3 h, and the reaction vessel is cooled over a period of 4 hours. The final product (CoNi-MOFs nanosheet arrays) is rinsed three times with ultrapure water and then dried at 60 °C for 9 hours. The corresponding Co-MOFs and Ni-MOFs can also be prepared according to the same conditions using the above-mentioned $Co(OH)_2$ and $Ni(OH)_2$ as precursors.

Synthesis of ZnNi-MOFs nanospheres

ZnNi-MOF nanospheres are synthesized by a modified method according to reference. [27] Briefly, 30 mg of zinc nitrate, 96 mg of nickel nitrate and 166 mg of 1,4-benzenedicarboxylic acid are dissolved in N, N-dimethylformamide (DMF) solution (20 mL) and ethylene glycol (6 mL) with stirring. After stirring for 50 min, the mixture is transferred into the Teflon liner of an autoclave and maintained at 130 °C for 6 h. Finally, the obtained precipitate, denoted as ZnNi-MOFs, is washed via centrifugation and dried at 60 °C overnight.

Synthesis of NB@ZnNi-MOFs spherical nanocomposites

In a typical process, 10 mg of NB is dissolved in 5 mL of deionized water under ultrasonication. After the dissolution of the reagents, 10 mg of ZnNi-MOFs is

dispersed into 5 mL of deionized water via stirred. Then, the NB solution is poured into the above solution and further stirred for 1 hour. Finally, the product is extensively washed with double-distilled water and ethanol via centrifugation until its filtrate is colorless, and dispersed in 2.5 mL of deionized water for further use.

Synthesis of the signal probe (HCG@BSA@HCG Ab_2@NB@ZnNi-MOFs)

The mixture solution of NB@ZnNi-MOFs (4 $mg \cdot mL^{-1}$, 1mL) and the solution of HCG Ab_2 (20 $\mu g \cdot mL^{-1}$, 1 mL) is shaken for 12 h at 4 °C. After incubated, BSA solution (1.0 wt%, 0.1 mL) is pipetted into the mixture solution to block the nonspecific sites, and then continue to be shaken for 3 hours at 4 °C. Subsequently, the resultant solution (BSA@HCG Ab_2@NB@ZnNi-MOFs) is centrifuged at 3000 rpm, carefully washed with PBS (pH = 7.4) to remove the unbound antibodies, then redisposed in 1 mL of PBS and stored at 4 °C. Finally, mixing different concentrations of HCG and BSA@HCG Ab_2@NB@ZnNi-MOFs (Keep excess) evenly to form the signal probe. The complete synthesis of the signal probe (HCG@BSA@HCG Ab_2@NB@ZnNi-MOFs) is shown in Scheme 1A.

Fabrication of immunosensor

The procedure of the preparing fabrication of the sandwich-type electrochemical immunosensor is demonstrated in Scheme 1B. Above all, 5.0 μL of 25 $\mu g \cdot mL^{-1}$ Ab1 solution is loaded on the surface of the film of CoNi-MOFs nanosheets at 4 °C for 50 min. Next,4.0 μL of BSA solution (1.0 wt%) is pipetted on the CoNi-MOFs nanosheet array-electrode, in order to prevent any possible nonspecific sites, and maintained it at

a constant temperature of 4 °C for about 30 min. Then, 5.0 μL of solution with a variety of signal probe n (HCG@BSA@HCG Ab_2@NB@ZnNi-MOFs) is loaded on the surface of CoNi-MOFs nanosheet array-electrode and incubated for 50 min at 37 °C to ensure the specific binding with HCG of the signal probe and HCG Ab_1. After each step, the designed electrode is washed with PBS (pH = 7.4) and stored at 4 °C for further use. The prepared immunosensor is tested by square wave voltammetry (SWV). The SWV scan is worked from -0.7 to 0.1 V with the square wave frequency of 15 Hz, and the square wave amplitude is 25 mV.

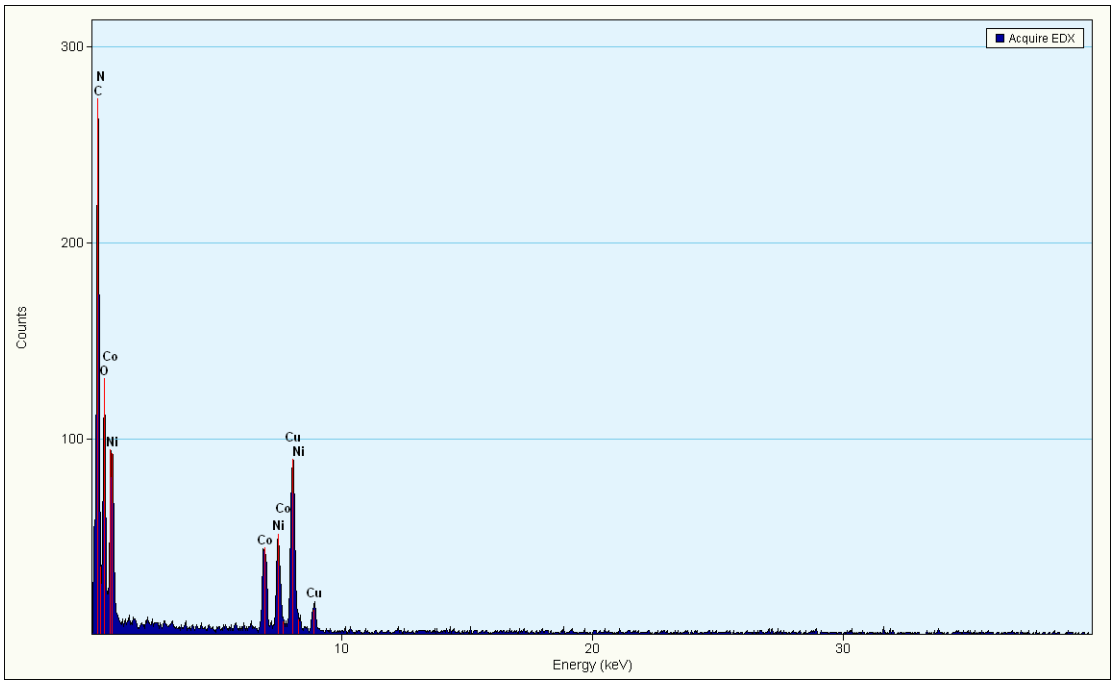

Figure S1. EDX spectrum of CoNi-MOFs nanosheets on the copper support film.

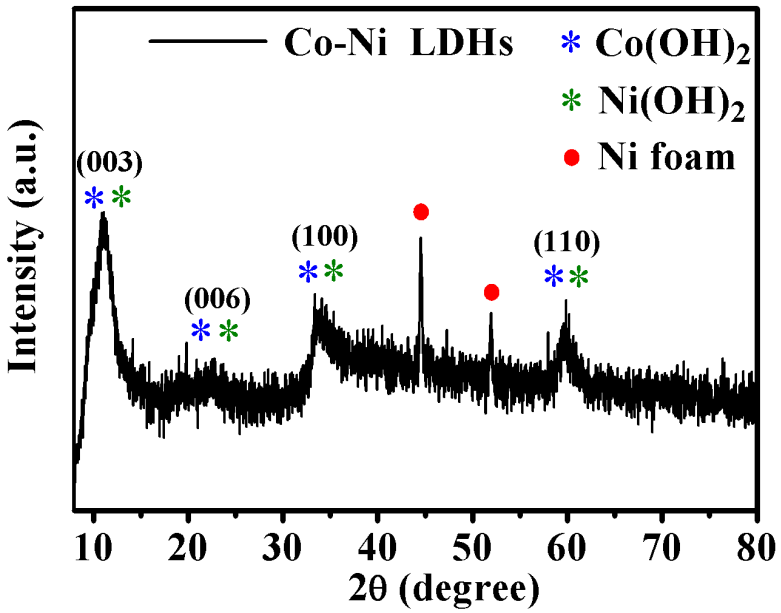

Figure S2. PXRD pattern of the Co-Ni LDHs.

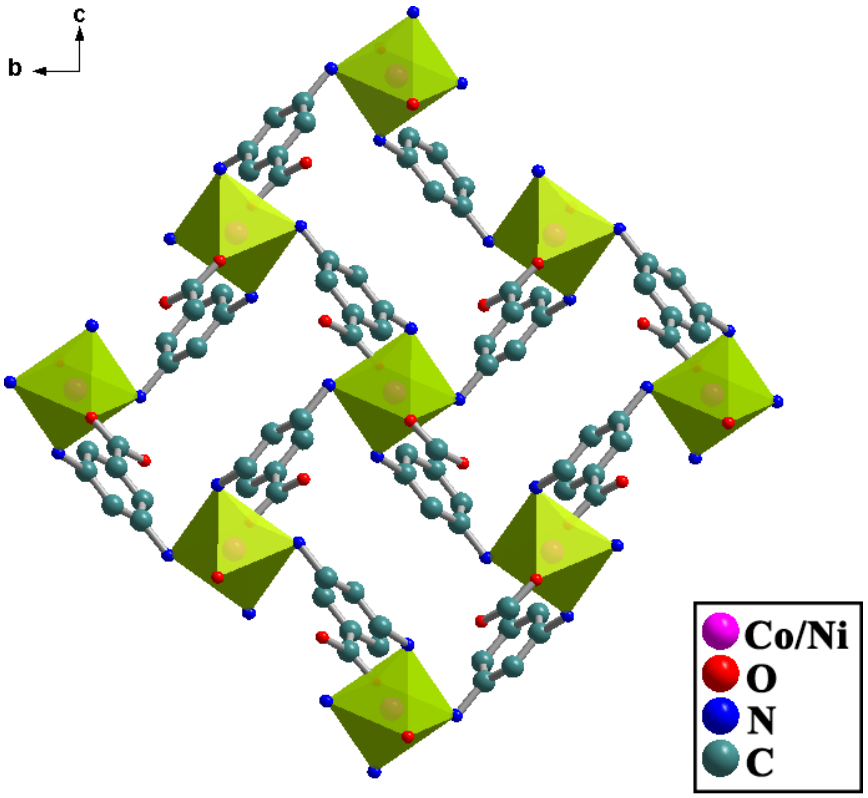

Figure S3. The schematic diagram of the crystal structure.

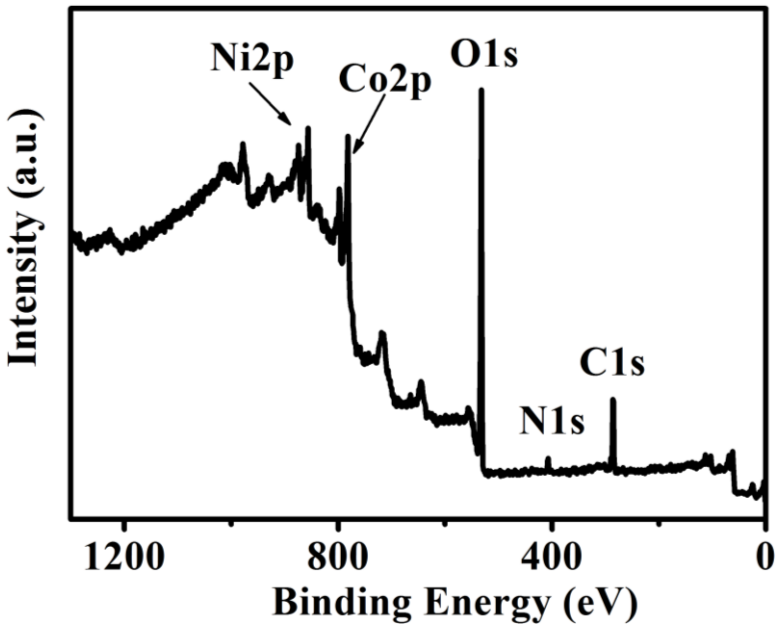

Figure S4. XPS survey spectrum of CoNi-MOFs nanosheets.

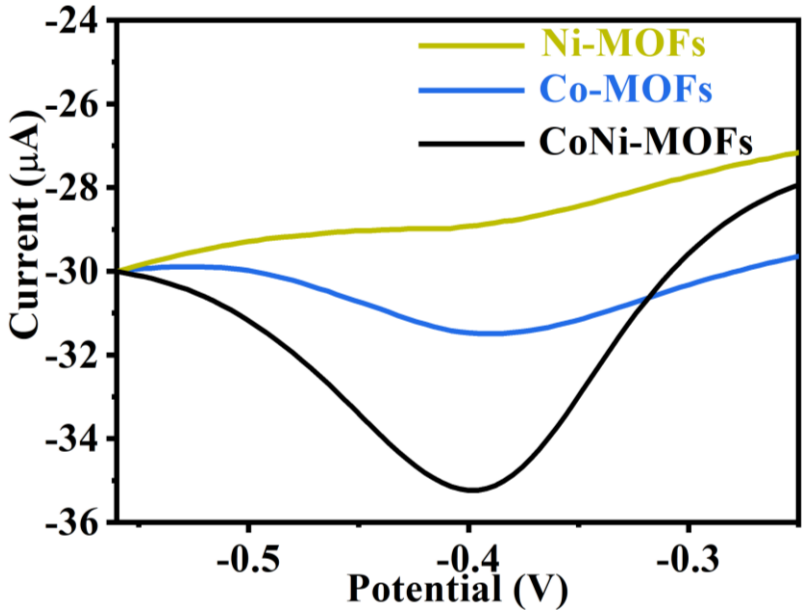

Figure S5. The SWV curves of Ni-MOFs (orange), Co-MOFs (blue) and CoNi-MOFs (black) collected at a square wave amplitude of 25 mV in 15.0 mL of PBS (pH=7.4).

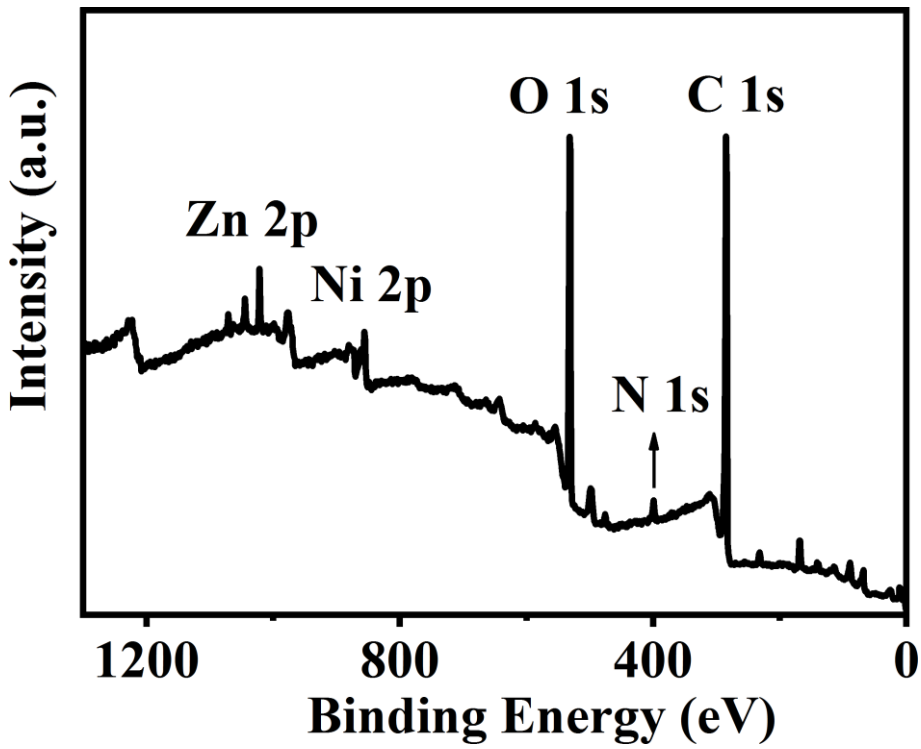

Figure S6. XPS survey spectrum of NB@ZnNi-MOFs.

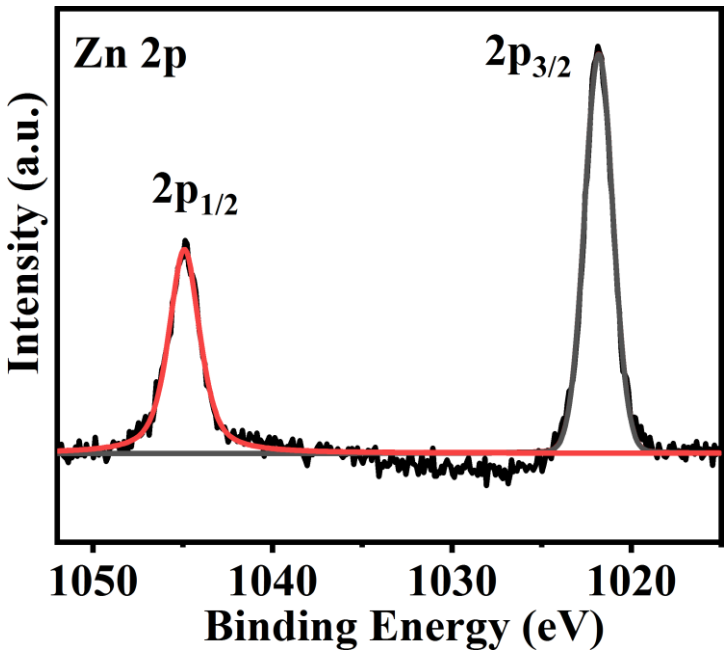

Figure S7. XPS spectra of Zn 2p core-level spectra in NB@ZnNi-MOFs.

The two bands in the Zn 2p spectrum correspond to transitions Zn $2p_{3/2}$ and Zn $2p_{1/2}$ at 1021.8 eV and 1044.9 eV, indicating that Zn^{2+} occur in the NB@ZnNi-MOFs.

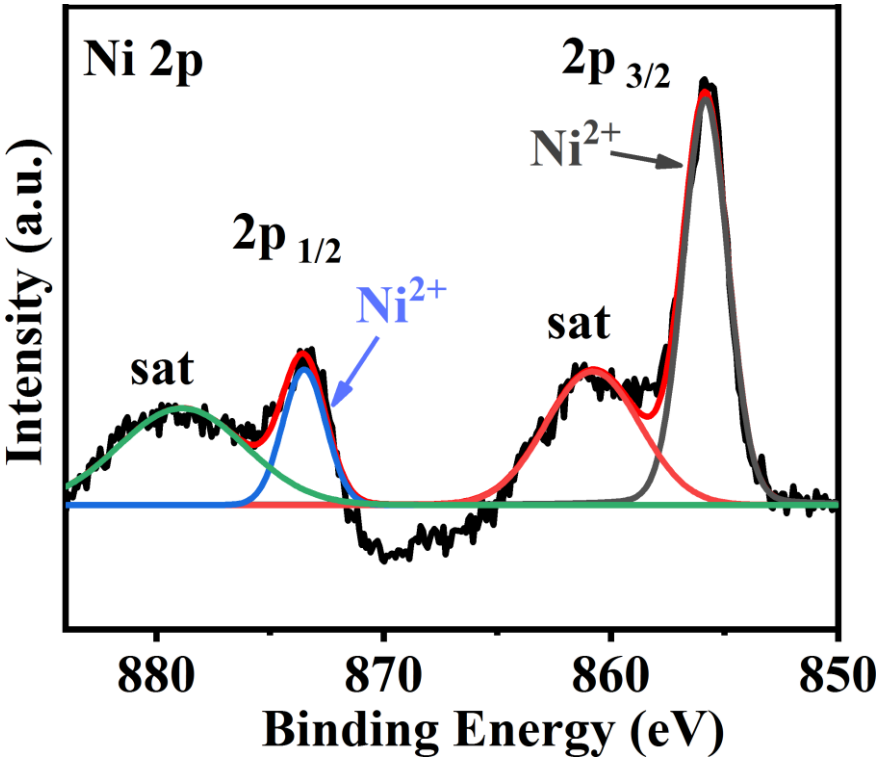

Figure S8. XPS spectra of Ni 2p core-level spectra in NB@ZnNi-MOFs.

The binding energies at 855.8 eV and 873.5 eV are assigned to Ni $2p_{3/2}$ and Ni $2p_{1/2}$, indicating that Ni^{2+} occurs in the NB@ZnNi-MOFs.

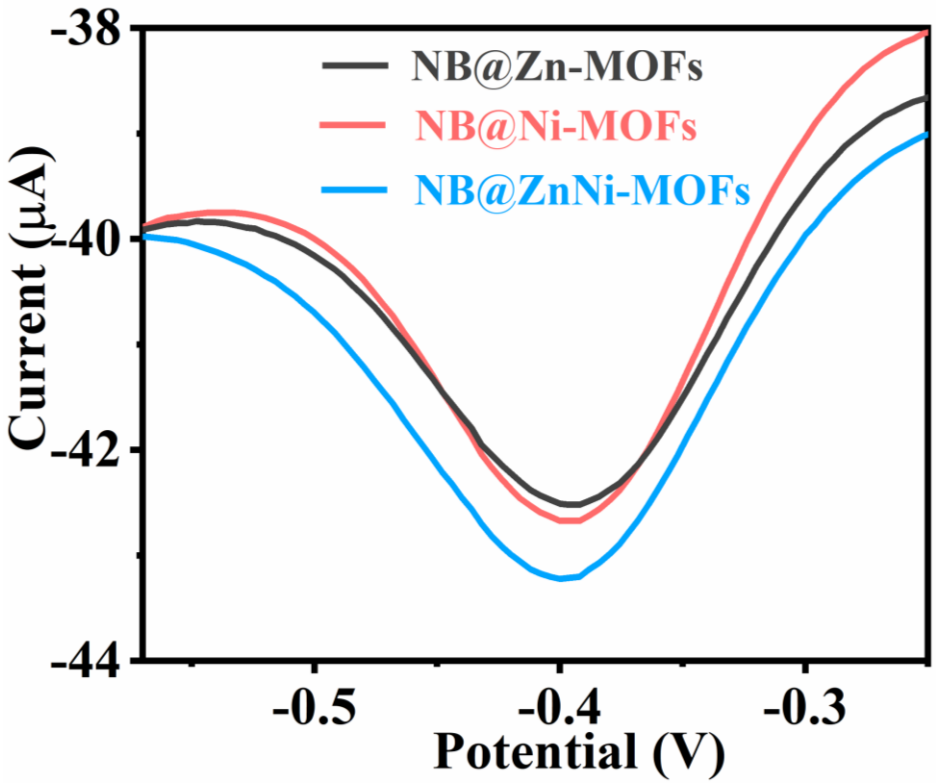

Figure S9. The SWV curves of NB@Zn-MOFs (black), NB@Ni-MOFs (pink) and NB@ZnNi-MOFs (blue) collected at square wave amplitude of 25 mV in 15.0 mL of PBS.

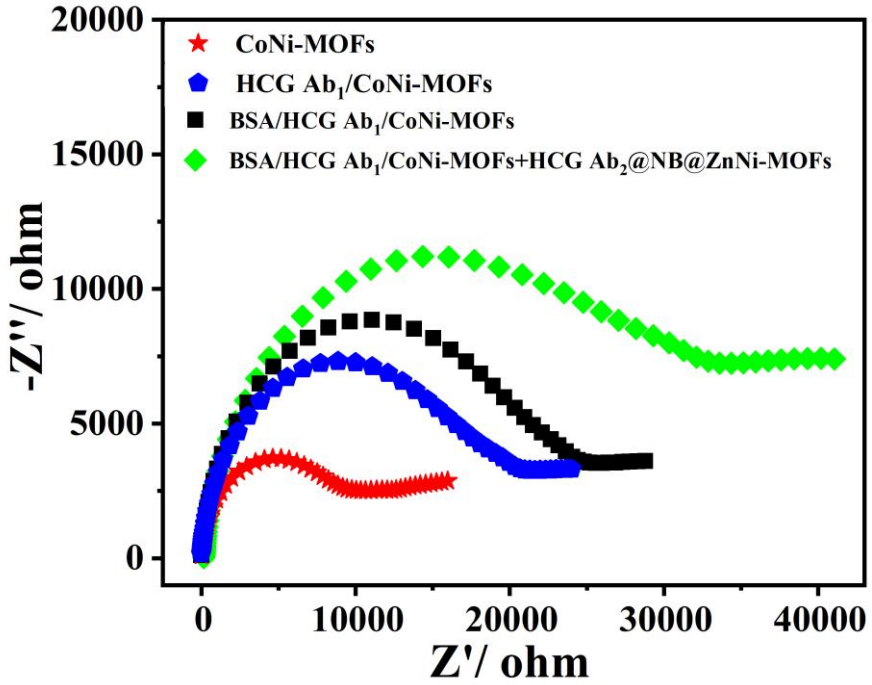

Figure S10. EIS of the different decorated electrodes in 1 mmol·L^{-1} $[Fe(CN)_6]^{3-/4-}$ and 0.1 mmol·L^{-1} KCl solution. This experiment is carried out on CoNi-MOFs nanosheet array decorated GCE.

When Ab1, BSA and signal probe was gradually used to modify on CoNi-MOFs nanosheet array/glassy carbon electrode (GCE), as shown in R4, the capacitive reactance increases gradually (cure b-d) along with the modification of electrodes layer by layer owing to the inhibition effect of protein on electronic conductivity, indicating this immunosensor has been successfully fabrication.

Table S1. Comparison of different methods for the detection of HCG.

Materials	Method	Linear ranges	Detection limits	Refs.
PLNPs	Lateral flow assay	0-10 ng · mL^{-1}	1 ng · mL^{-1}	[1]
AgNPs	LSV	1-200 mIU · mL^{-1}	0.4 mIU · mL^{-1}	[2]
Au/AgNPs	Colorimetrc detection	0.01-100 ng · mL^{-1}	10.8 pg · mL^{-1}	[3]
Au NPs@LPCs-SnS_2	CV	0.5-50 ng · mL^{-1}	6.4 pg · mL^{-1}	[4]
graphene oxide-peptide-based surface plasmon	surface plasmon resonance	0.065-8.32 nM	0.065 nM	[5]
NB@ZnNi-MOFs sphere and CoNi-MOFs nanosheet array	SWV	0.001-50 ng · mL^{-1}	0.37 pg · mL^{-1}	This method

References

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