

## Electronic Supplementary Information

### Magnetic nanoparticles assisted sensitive detection of nitrated $\alpha$ -syn in blood based on sensitizing electrochemical layer

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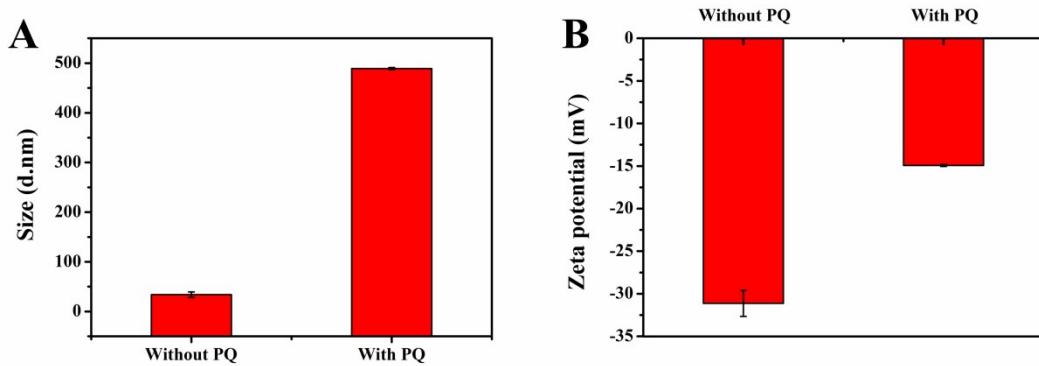
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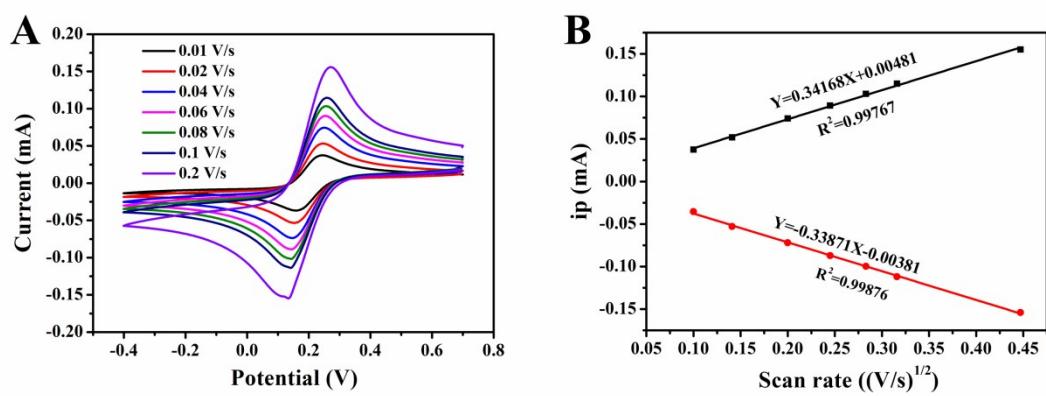
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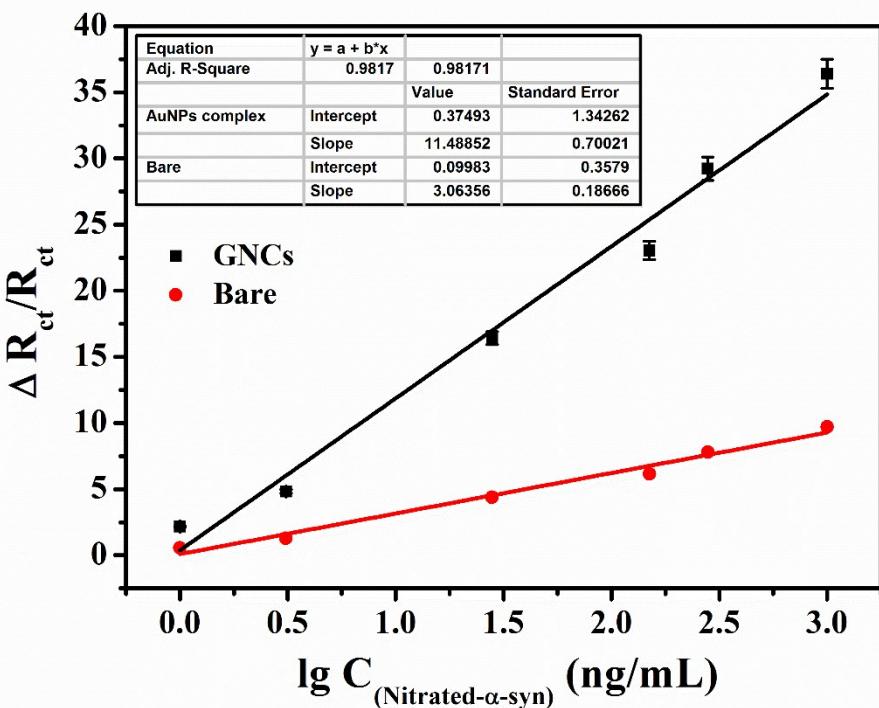
<sup>‡</sup>These authors contributed equally to this work.



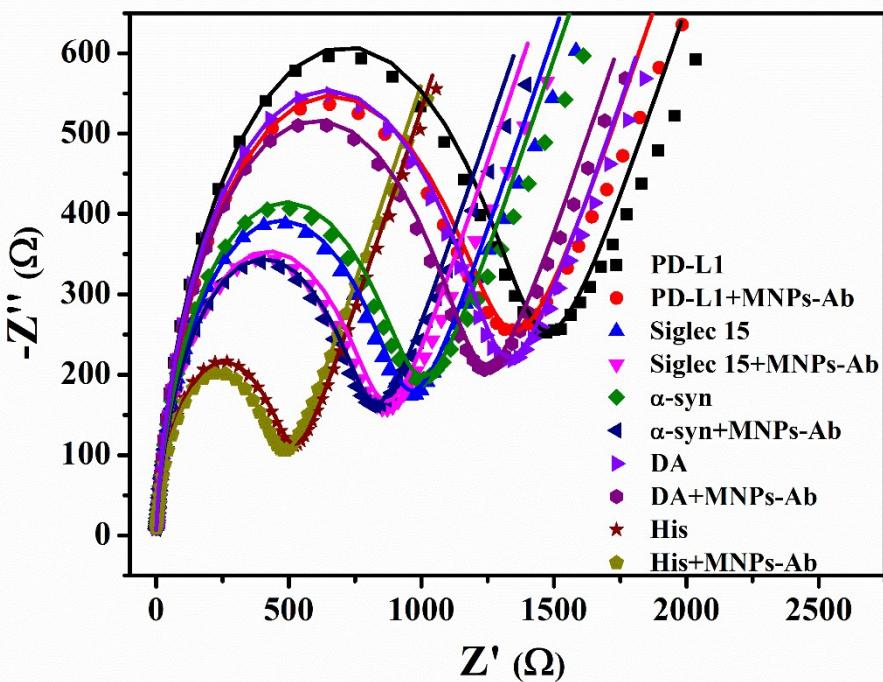
**Fig. S1.** Dynamic light scattering (A) and zeta potential results (B) of AuNPs with or without PQ.



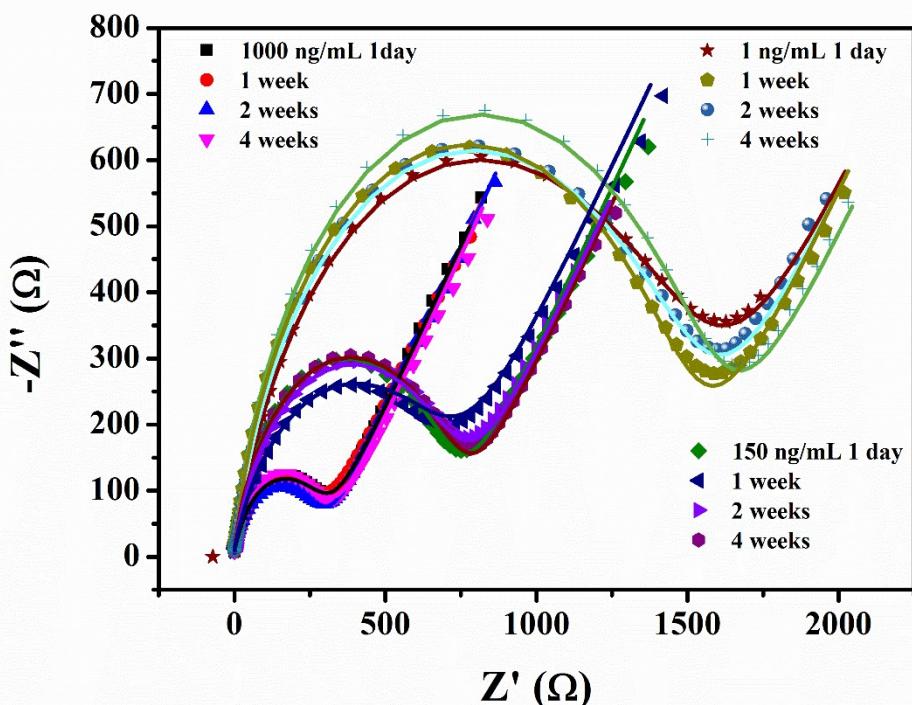
**Fig. S2.** (A) Diffusion control process for bare gold electrode, and (B) corresponding calibration curves.



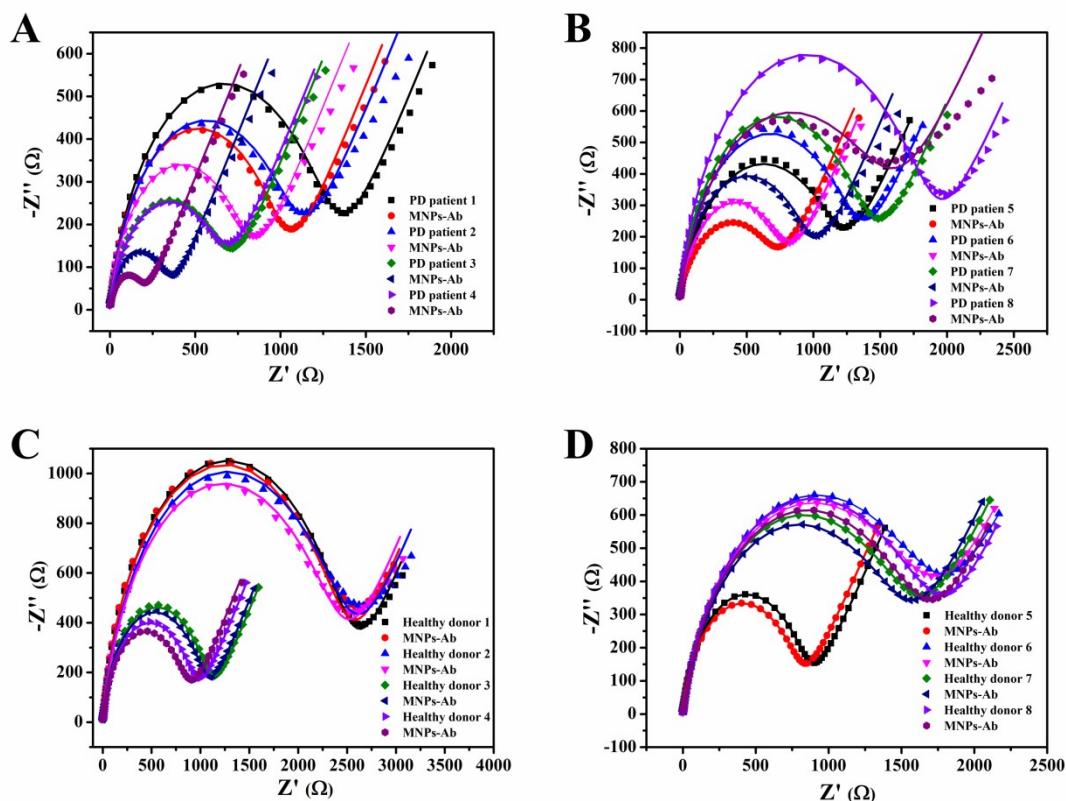
**Fig.S3.** The relationship between the electrode resistance response and the logarithm of nitrification  $\alpha$ -syn concentration under different background signals.



**Fig. S4.** EIS diagram in the process of detecting interfering substances of nitrated  $\alpha$ -syn.



**Fig. S5.** EIS diagram of detecting different concentrations of nitrated  $\alpha$ -syn in different store time (1 day, 1 week, 2 weeks, 4 weeks).



**Fig. S6.** EIS diagram for the determination of healthy donors ( $n=8$ ) and PD patients ( $n=8$ ).

**Table S1.** Performance comparison of various neurological disease markers biosensors

| Method                | Biomarker                    | Linear range<br>(pg/mL)                   | LOD<br>(pg/mL)     | Reference    |
|-----------------------|------------------------------|---|--------------------|--------------|
| Electrochemical assay | Tau protein                  | $1.1 \times 10^7$ - $200 \times 10^6$     | $1.1 \times 10^7$  | <sup>1</sup> |
| Electrochemical assay | Tau protein                  | $0.55$ - $5.5 \times 10^5$                | 1.65               | <sup>2</sup> |
| Electrochemical assay | Tau protein                  | $1.375 \times 10^4$ - $1.375 \times 10^7$ | $8.25 \times 10^3$ | <sup>3</sup> |
| Electrochemical assay | Myelin Basic Protein         | $9.259 \times 10^3$ - $9.259 \times 10^6$ | $5.55 \times 10^3$ | <sup>3</sup> |
| Electrochemical assay | Amyloid-beta 1-42            | $500$ - $5 \times 10^5$                   | 100                | <sup>4</sup> |
| Electrochemical assay | $\alpha$ -synuclein          | $1 \times 10^4$ - $1 \times 10^6$         | $3.62 \times 10^3$ | <sup>5</sup> |
| Electrochemical assay | $\alpha$ -synuclein oligomer | $864$ - $3.11 \times 10^8$                | 144                | <sup>6</sup> |
| Electrochemical assay | Nitrated $\alpha$ -syn       | $1000$ - $1 \times 10^6$                  | 310                | This work    |

**Table S2.** Measurement of nitrated  $\alpha$ -syn in fetal bovine serum with the designed sensor.

| Sample | Added<br>(ng/mL) | Theoretical     | Actual          | Recovery | RSD (%) |
|--------|------------------|-----------------|-----------------|----------|---------|
|        |                  | $\Delta R_{ct}$ | $\Delta R_{ct}$ | (%)      |         |
| 1      | 2                | 153             | 145             | 94.7     | 4.57%   |
| 2      | 3                | 219             | 198             | 90.4     | 2.41%   |
| 3      | 20               | 612             | 562             | 91.8     | 6.31%   |

**Table S3.** Information of clinical serum samples.

| Patient ID | Gender | Age (y) | Clinical Investigations                      | Serum time |
|------------|--------|---------|--|------------|
| 1          | Male   | 58      | Parkinson's Disease                          | 12/8/2020  |
| 2          | Female | 74      | Parkinson's disease, cerebrovascular disease | 12/8/2020  |
| 3          | Male   | 68      | Parkinson's Disease                          | 12/10/2020 |
| 4          | Female | 79      | Primary parkinsonism                         | 12/8/2020  |
| 5          | Female | 53      | Parkinson's Disease                          | 12/16/2020 |
| 6          | Female | 33      | Parkinson's Disease                          | 12/17/2020 |
| 7          | Male   | 78      | Parkinson's Disease                          | 12/25/2020 |
| 8          | Male   | 72      | Parkinson's Disease                          | 1/5/2021   |
| Donor ID   | Gender | Age (y) | Clinical Investigations                      | Serum time |
| 1          | Male   | 59      | Diabetes                                     | 1/8/2021   |
| 2          | Female | 71      | Urinary Tract Infection                      | 1/8/2021   |
| 3          | Female | 73      | Diabetes                                     | 1/7/2021   |
| 4          | Female | 73      | Diabetes                                     | 1/4/2021   |
| 5          | Female | 73      | /  | 1/6/2021   |
| 6          | Female | 78      | Arthritis                                    | 1/6/2021   |
| 7          | Male   | 78      | Stomach cancer                               | 1/4/2021   |
| 8          | Male   | 73      | Arthritis                                    | 1/4/2021   |

## Reference

- 1 E.-V. Jose O., T. Hanna and M. Sanel, *Analyst*, 2014, **139**, 2823-2831.
- 2 S. X. Wang, D. Acha, A. J. Shah, F. Hills, I. Roitt, A. Demosthenous and M. Sanel, *Biosens. Bioelectron.*, 2016, **92**, 482-488.
- 3 B. Derkus, P. A. Bozkurt, M. Tulu, K. C. Emregul, C. Yucesan and E. Emregul, *Biosens. Bioelectron.*, 2017, **89**, 781-788.
- 4 E. C. Rama, M. B. González-García and A. Costa-Garcia, *Sens. Actuators B Chem.*, 2014, **201**, 561-571.
- 5 C. Y. Ge, M. M. Rahman, W. Zhang, N. S. Lopa, K. Jin, S. Yoon, H. Jang, G. R. Xu and W. Kim, *Sensors*, 2020, **20**, 617.
- 6 S. M. Taghdisi, N. M. Danesh, M. A. Nameghi, M. Ramezani, M. Alibolandi, M. Hassanzadeh-Khayat, A. S. Emrani and K. Abnous, *Biosens. Bioelectron.*, 2019, **123**, 14-18.