Supporting Information

Zn(II)-based tyramine-conjugated porphyrin complex as an active tyrosinase inhibitor for potential neuroprotection by improving the mitochondrial homeostasis

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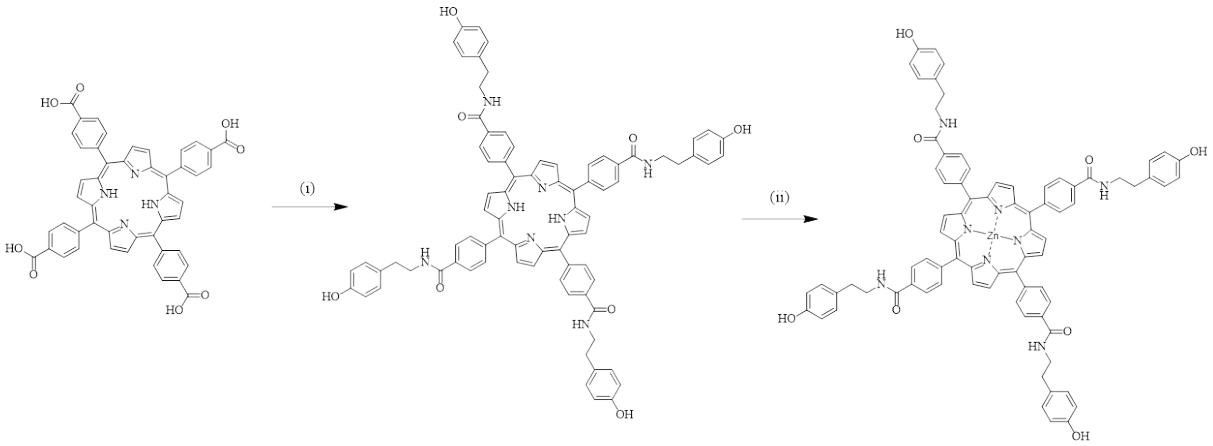

TCPP **P4TA** **ZnP4TA**

Scheme S1. Synthesis procedures of P4TA and ZnP4TA. Reagents and conditions: i) pyridine, tyramine, HOBT, EDCI, DIPEA, RT, 8 h; ii) MeOH, $Zn(CH3COO)_2$, 90 ^oC, reflux, 6 h.

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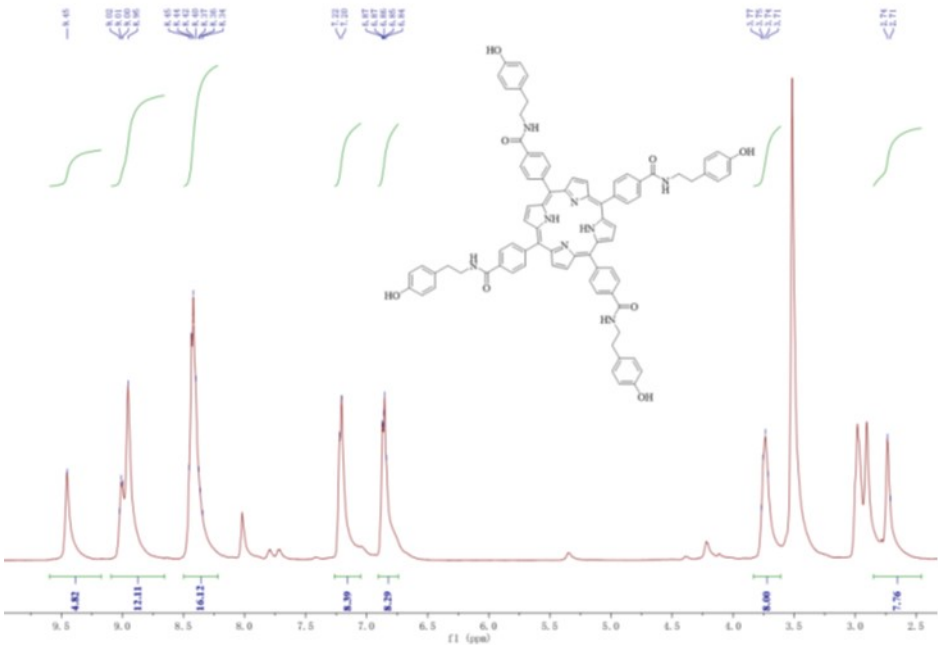

42 **Figure S1.** ^{1}H NMR spectrum of P4TA in ^{7}d-DMF.

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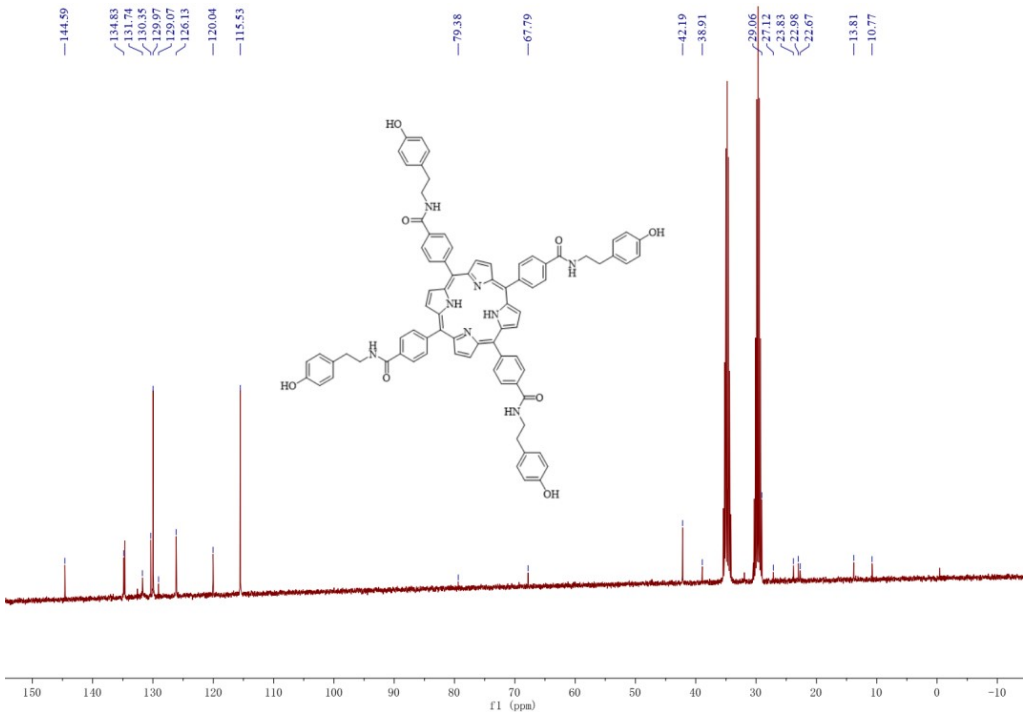

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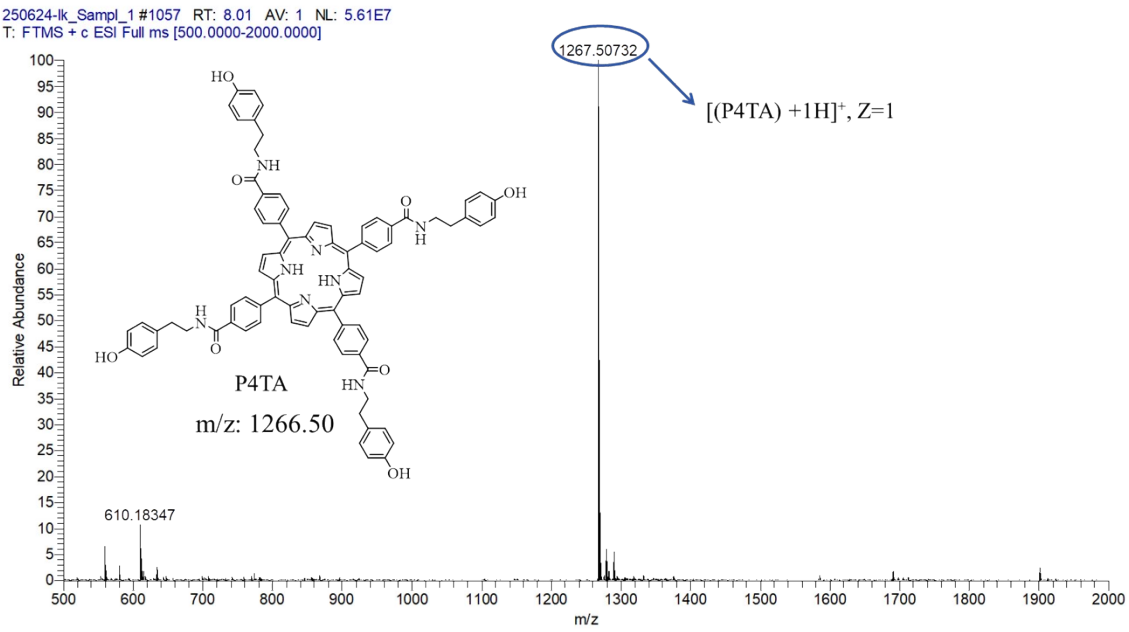
45 **Figure S2.** ^{13}C NMR spectrum of P4TA in ^{7}d-DMF.



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47 **Figure S3.** High-resolution mass spectrometry of P4TA in methanol.

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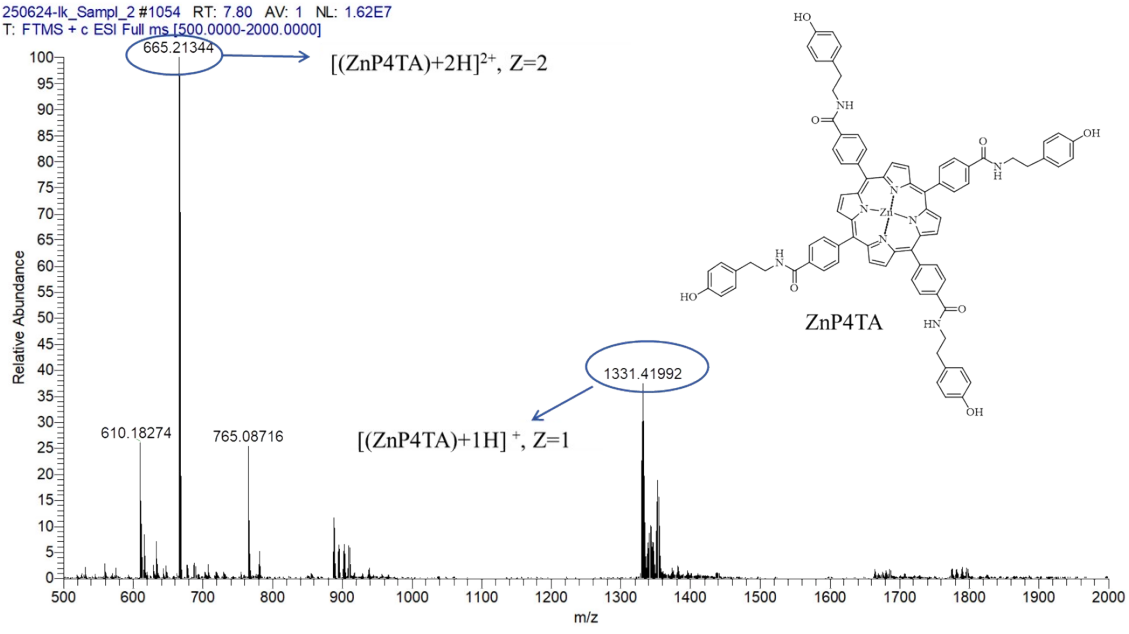

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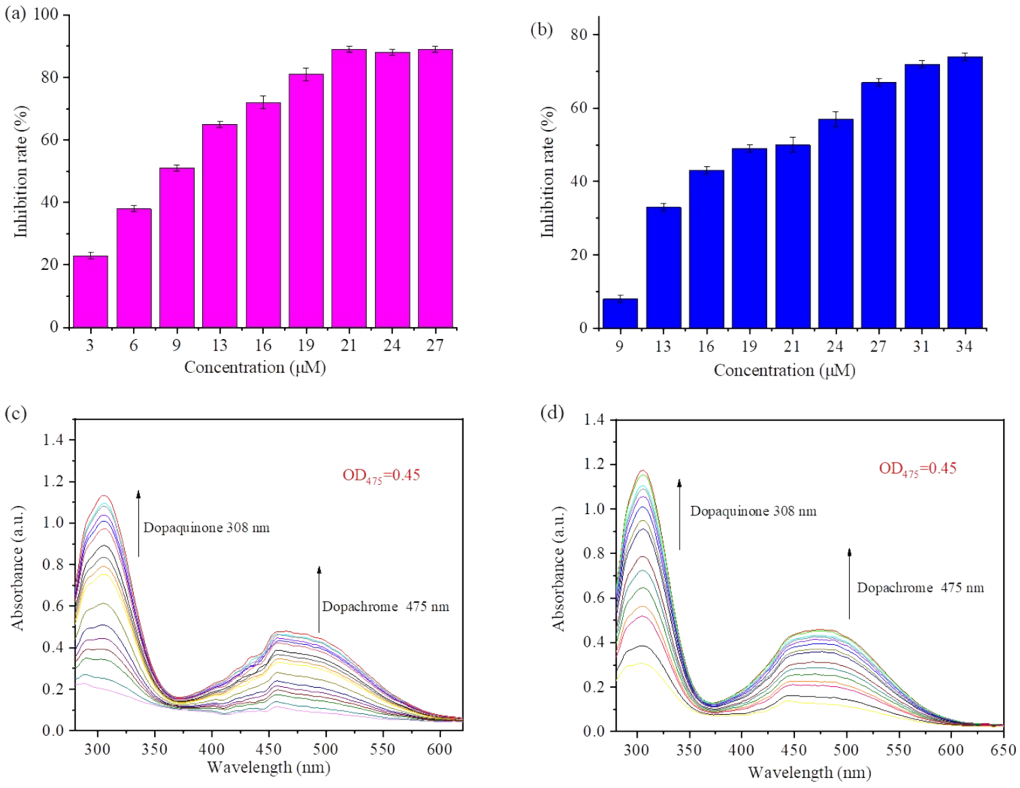
50 **Figure S4.** High-resolution mass spectrometry of ZnP4TA in methanol.



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52 **Figure S5.** (a) Inhibitory percentage of TYR by P4TA at concentrations of 3 to 27 μM, and (c) by

53 ZnP4TA at concentrations of 9 to 34 μM; (b) UV absorption spectra of L-Tyr catalyzed by TYR

54 over 17 min at the IC_{50} of P4TA, and (d) at the IC_{50} of ZnP4TA.

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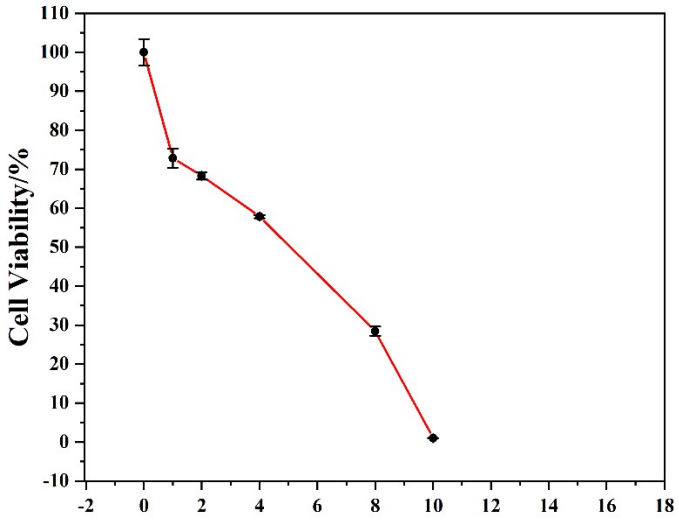

Figure S6A. The cell viability of SH-SY5Y cells after treated with different concentration of RO (0-10 μM).

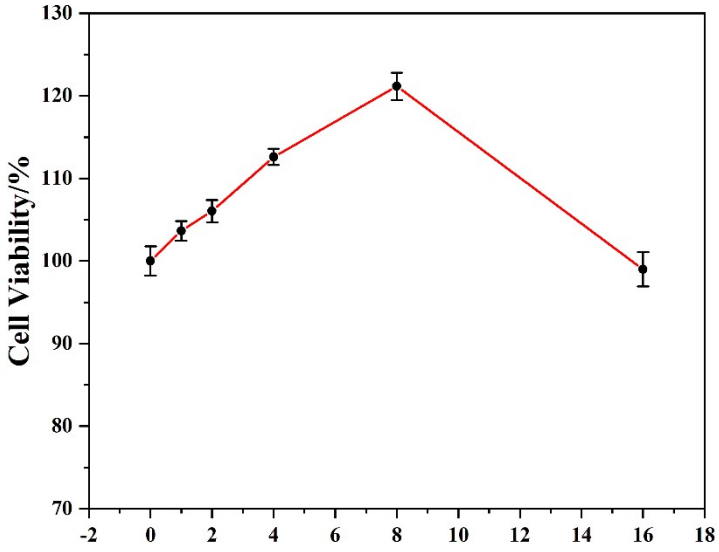

Figure S6B. The cell viability of SH-SY5Y cells after treated with different concentration of ZnP_4TA (0-16 μM).

Table S1. The UV-Vis value of A_1 ~ A_4 regarding the inhibition rate of P4TA.

P4TA (μM)	3	6	9	13	16	19	21	24	27
A_1	0.90	0.90	**0.90**	0.90	0.90	0.90	0.90	0.90	0.90
A_2	0.02	0.02	**0.02**	0.02	0.02	0.02	0.02	0.02	0.02
A_3	0.68	0.55	**0.43**	0.38	0.33	0.28	0.26	0.31	0.36
A_4	0	0	**0**	0.07	0.09	0.12	0.16	0.2	0.26
I (%)	22.72	37.53	**50.61**	64.94	72.31	81.32	89.13	87.63	88.63

Table S2. The UV-Vis value of A_1 ~ A_4 regarding the inhibition rate of ZnP4TA.

ZnP4TA (μM)	9	13	16	19	21	24	27	31	34
A_1	0.90	0.90	0.90	0.90	**0.90**	0.90	0.90	0.90	0.90
A_2	0.02	0.02	0.02	0.02	**0.02**	0.02	0.02	0.02	0.02
A_3	0.89	0.82	0.75	0.65	**0.56**	0.54	0.55	0.54	0.53
A_4	0	0	0	0	**0.06**	0.08	0.13	0.16	0.2

I (%)	8.29	33.33	42.53	49.43	**49.98**	56.96	67.23	72.36	73.56

Table S3. Fitted parameters from luminescent spectra via P4TA and ZnP4TA titrations by TYR.

Compound	Binding target	*Ka (mL/μM)	n	R^2
ZnP4TA	Tyrosine motifs	4.41	0.60	0.99
P4TA		1127	1.87	0.97
ZnP4TA	tryptophan motifs	14.86	0.92	0.98
P4TA		51.02	0.96	0.97

* $\lg\left[\frac{(F_0 - F)}{F}\right] = \lg Ka + n\lg[Q]$