Supporting information

Ruthenium complexes as inhibitors of human islet amyloid polypeptide aggregation, an effect that prevents beta cell apoptosis

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1. Methods.

Synthesis and characterization of the Ru complexes.

The Ru complexes were prepared by literature methods with slight changes and the result we got is same as the reported literature[1-5]. here we described a simplified syntfesis method. 1 mmol Hydrated rutrichloride (0.26 g) and 1.5 mmol the diimine ligands (bpy,0.24 g; phen, 0.27 g, pip, 0.43 g, phtpy,0.51 g) were mixed and stirred for 3 h at 80 ℃ until the solution colour no longer changed. After that, the solution were added a saturated aqueous $NaClO_4$ solution, then filtered off and dried in vacuo. The products were then purified by alumina column chromatography with toluene and methanol as eluant.

1.1. NAMI-A (**1**)

The complex NAMI-A was prepared according to the above procedure and get the same results as the reported literature[1]. Yield 0.645 g, 55.8%.

1.2. $[Ru(bpy)_3](ClO_4)_2$ (**2**)

The complex $[Ru(bpy)_3](ClO_4)_2$ was prepared according to the above procedure and get the same results as the reported literature[2]. Yield 0.428 g, 75.8%. $[Ru(bpy)_3](ClO_4)_2$ $C_{30}H_{24}Cl_2N_6O_8Ru$ Anal. Calc. for $C_{30}H_{24}C_{l2}N_6O_8Ru$:C 46.88, H 3.15,N 10.94. Found: C 46.94, H 3.41, N 10.81%.

1.3 $[Ru(pip)_3](ClO_4)_2$ (**3**)

The complex $[Ru(pip)_3](ClO_4)_2$ was prepared according to the above procedure and get the same results as the reported literature.[3] Yield 0.422 g, 58.4%. Anal. Calc. for $C_{57}H_{36}C_{l2}N_{12}O_8Ru$: C, 57.58; H, 3.05; N, 14.14; Ru, 8.50; found (%): C, 57.56; H, 3.06; N, 14.15.

1.4.$[Ru(phtpy)(phen)Cl]ClO_4$ (**4**)

The complex $[Ru(phtpy)(phen)Cl]ClO_4$ was prepared according to the above procedure and get the same results as the reported literature[4]. Yield 0.388 g, 42.4%.Anal. Calc. for $C_{33}H_{23}C_{l2}N_5O_4Ru$:C 54.63, H 3.20,N 9.65. Found: C 54.39, H 3.41, N 9.71%.

2. Results

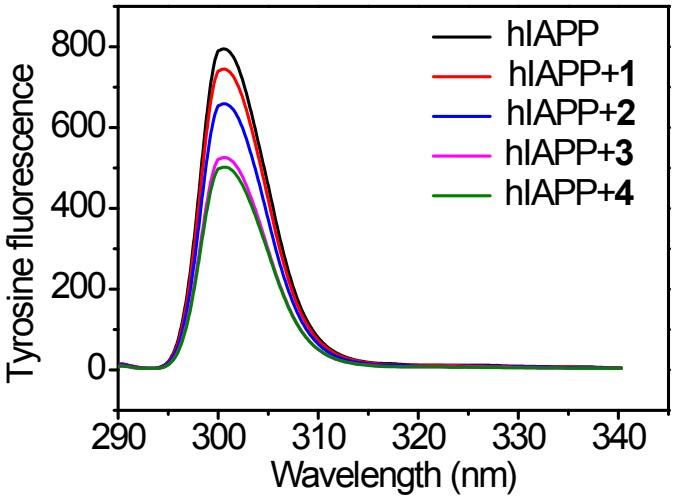

Figure S1 The Tyrosine fluorescence intensity of 10 μM hIAPP after incubation in the absence or presence of 5 μM Ru complexes in the dark room.

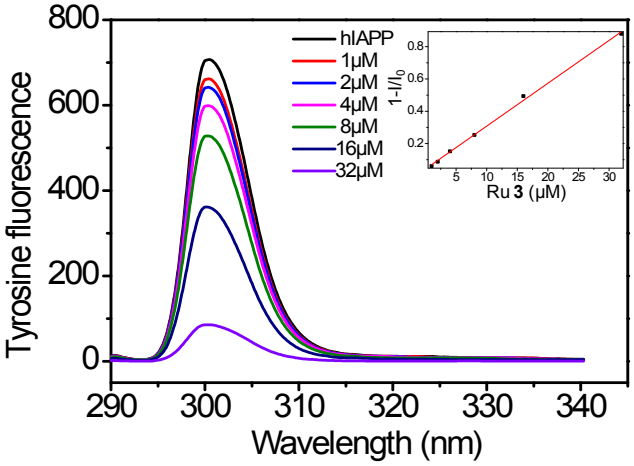

Figure S2. Tyrosine fluorescence intensity of hIAPP after incubation in the absence or presence of different concentration of complex **3.**

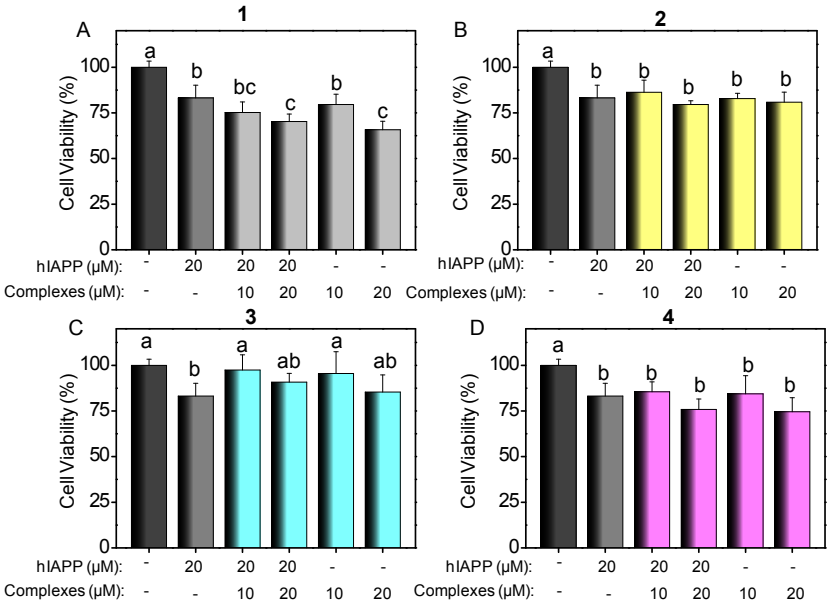

Figure S3. Dose-dependent protective effects of Ru complexes against hIAPP. was incubated with different concentrations of complexes **1**(A), **2**(B), **3**(C) and **4**(D) in INS-1 cells at 37 ℃ for 48 h. Bars with different characters are statistically different at $P<0.05$ level as analyzed by one-way ANOVA multiple comparison.

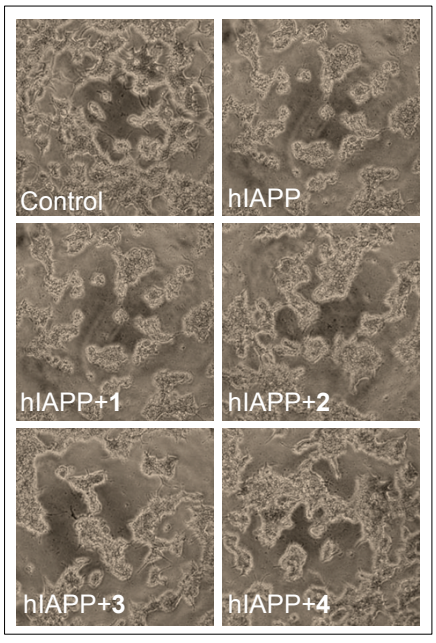

Figure S4. Morphological changes induced by hIAPP and the protective effects of Ru complexes. The cells were treated with 20 μM hIAPP in combination with 5 μM Ru complexes **1**, **2**, **3** and **4** at 37 ℃ for 48 h. Magnification: 100 ×.

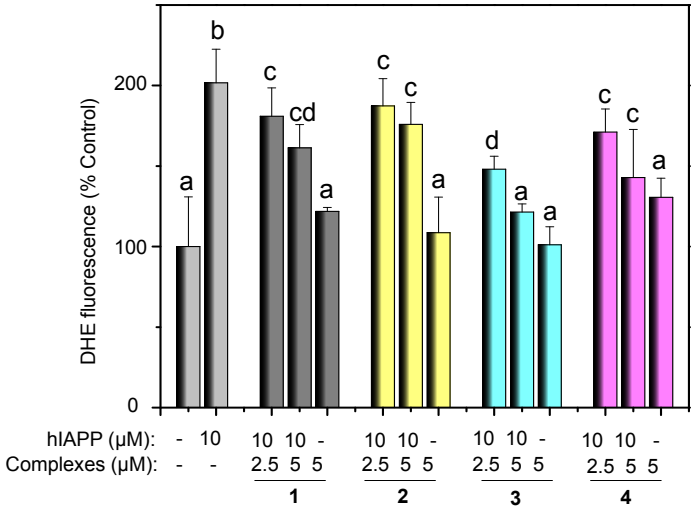

Figure S5. Ru complexes reduce ROS generation induced by hIAPP. INS-1 cells were incubated with hIAPP (10 μM) alone or with different Ru complexes (5 μM) at 37 ℃ for 60 min. Changes in ROS level was determined by DHE fluorescence intensity. The fluorescence intensity of control that treated without hIAPP and Ru complexes was expressed as 100%. The Values represented were means ±SD from three independent experiments. Bars with different characters are statistically different at $P<0.05$ level as analyzed by one-way ANOVA multiple comparison.

References

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