SUPPLEMENTARY INFORMATION

The effects of Platinum (IV) complex on Aβ $_{1\text{-}42}$ aggregation: a synergistic inhibition upon axial coordination

Sara La Manna[1], Daniele Florio[2], James A. Platts[3], Elisabetta Gabano[4], Mauro Ravera[5] and Daniela Marasco[1,]*

[1]Department of Pharmacy, University of Naples Federico II, 80131, Naples, Italy

[2]IRCCS SYNLAB SDN, Via G., Ferraris 144, 80146, Naples, Italy

[3]School of Chemistry, Cardiff University, Park Place Cardiff CF10 3AT UK

[4]Department of Sustainable Development and Ecological Transition, University of Piemonte Orientale, Piazza S. Eusebio 5, 13100, Vercelli, Italy

[5]Department of Sciences and Technological Innovation, University of Piemonte Orientale, Viale Michel 11, 15121 Alessandria, Italy

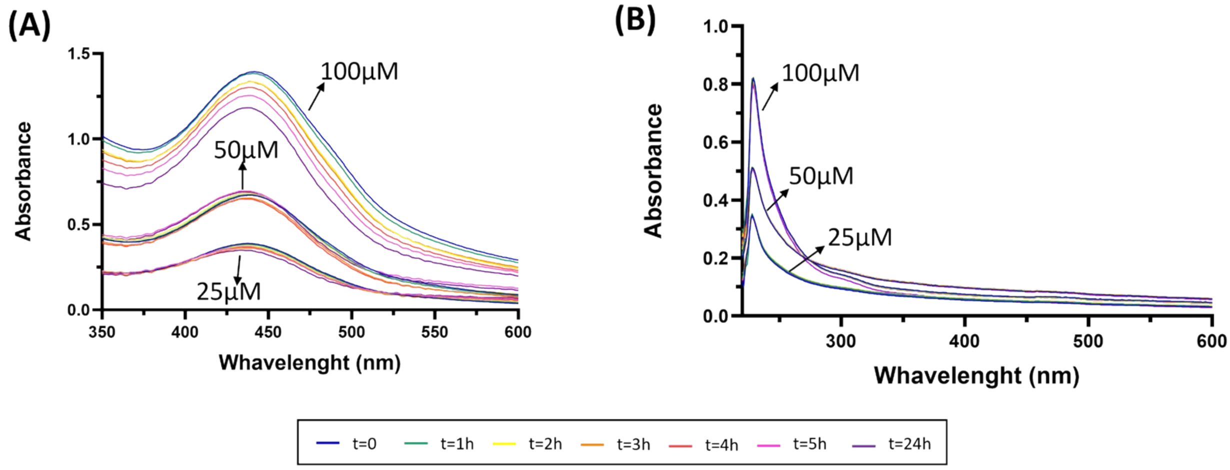

Figure S1. Stability overtime of A) **Pt-Ac-rhein** and B) **Pt-Ac-OH**, in 10 mM phosphate buffer at pH 7.4 (0.2% DMSO, v/v). 25, 50 and 100μM.

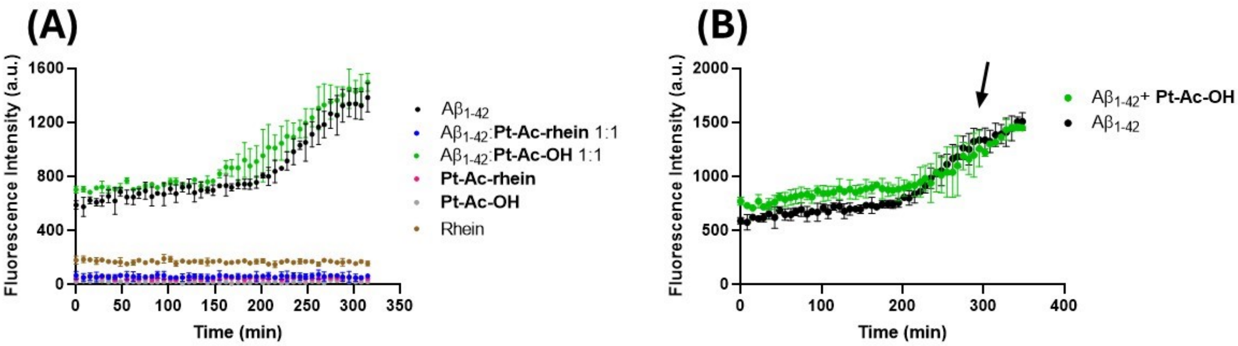

Figure S2: Overlay of time-courses of ThT fluorescence emission intensity of A) $A\beta_{1-42}$, in the absence and in the presence of **Pt-Ac-rhein**, **Pt-Ac-OH** and rhein and compounds alone, and B) upon the addition (indicated by an arrow) of the complexes at 1:1 ratio to preformed amyloid aggregates. The results are representative of two independent measurements

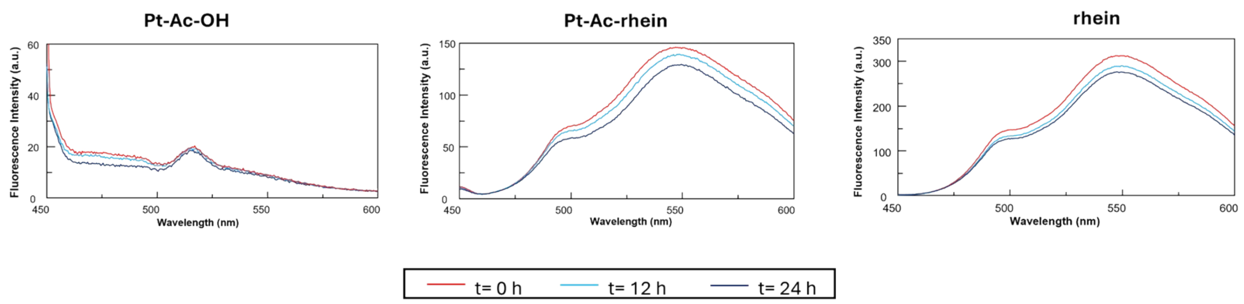

Figure S3. Fluorescence emission spectra at different times of Pt complexes and rhein (Λ_{ex} = 440 nm).

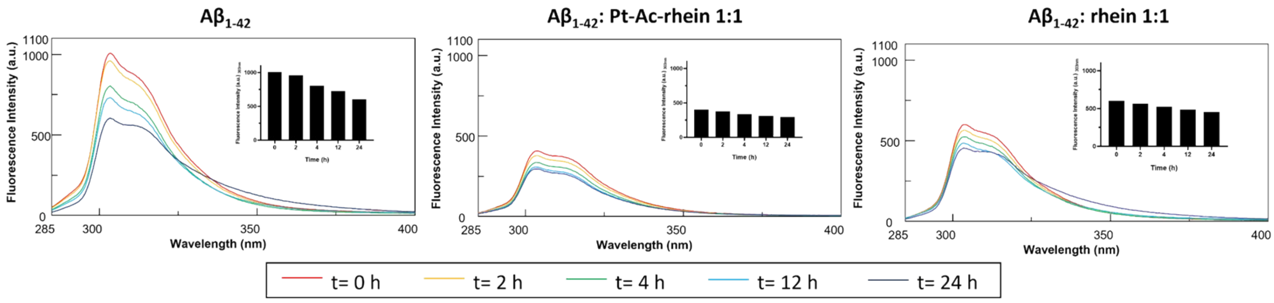

Figure S4. Fluorescence emission spectra at different times of $A\beta_{1-42}$ in the absence and presence of compound **Pt-Ac-rhein** or rhein. (Λex = 275 nm). As insets intensity at 303 nm versus time. $A\beta_{1-42}$ at 50 µM with the compounds at 1:1 molar ratio

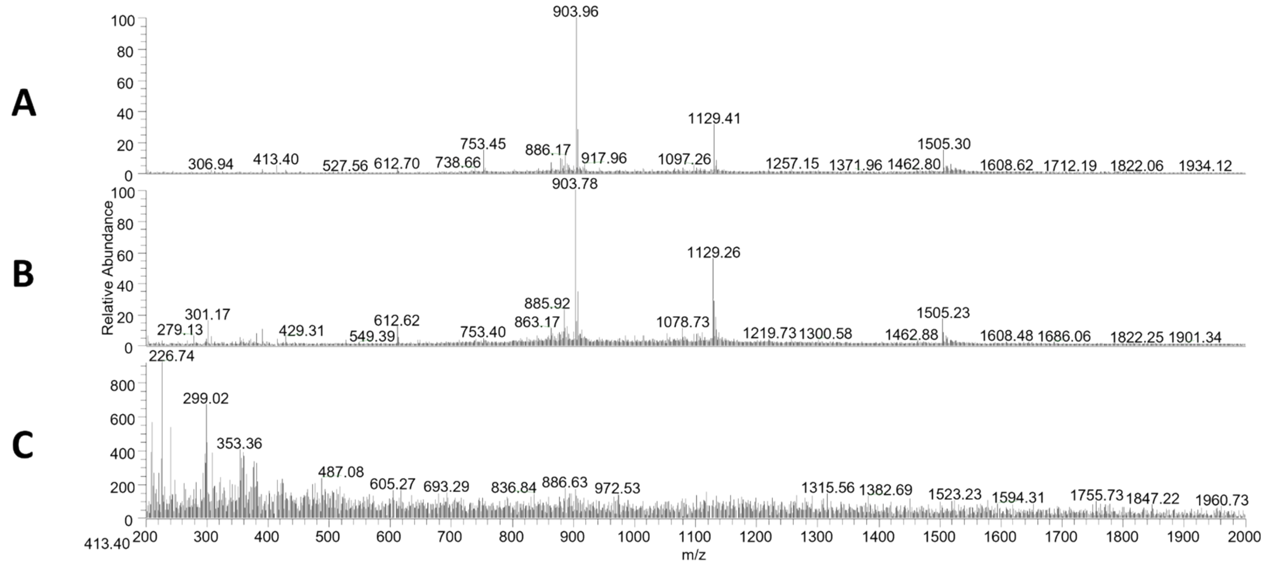

Figure S5. ESI-MS spectra of: A) A$\beta_{1\text{-}42}$ alone, B) A$\beta_{1\text{-}42}$ in presence of **Pt-Ac-OH** (at 1:1 molar ratio) and C) **Pt-Ac-OH** alone.

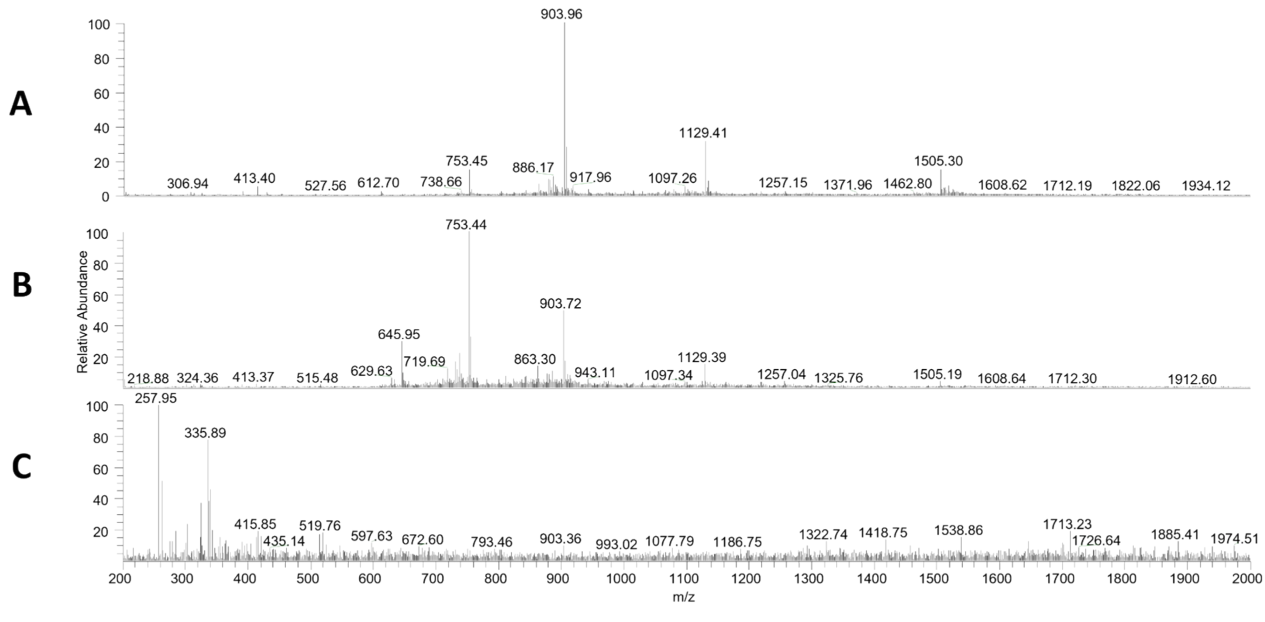

Figure S6. ESI-MS spectra of: A) A$\beta_{1\text{-}42}$ alone, B) A$\beta_{1\text{-}42}$ in presence of rhein (at 1:1 molar ratio) and C) rhein alone.

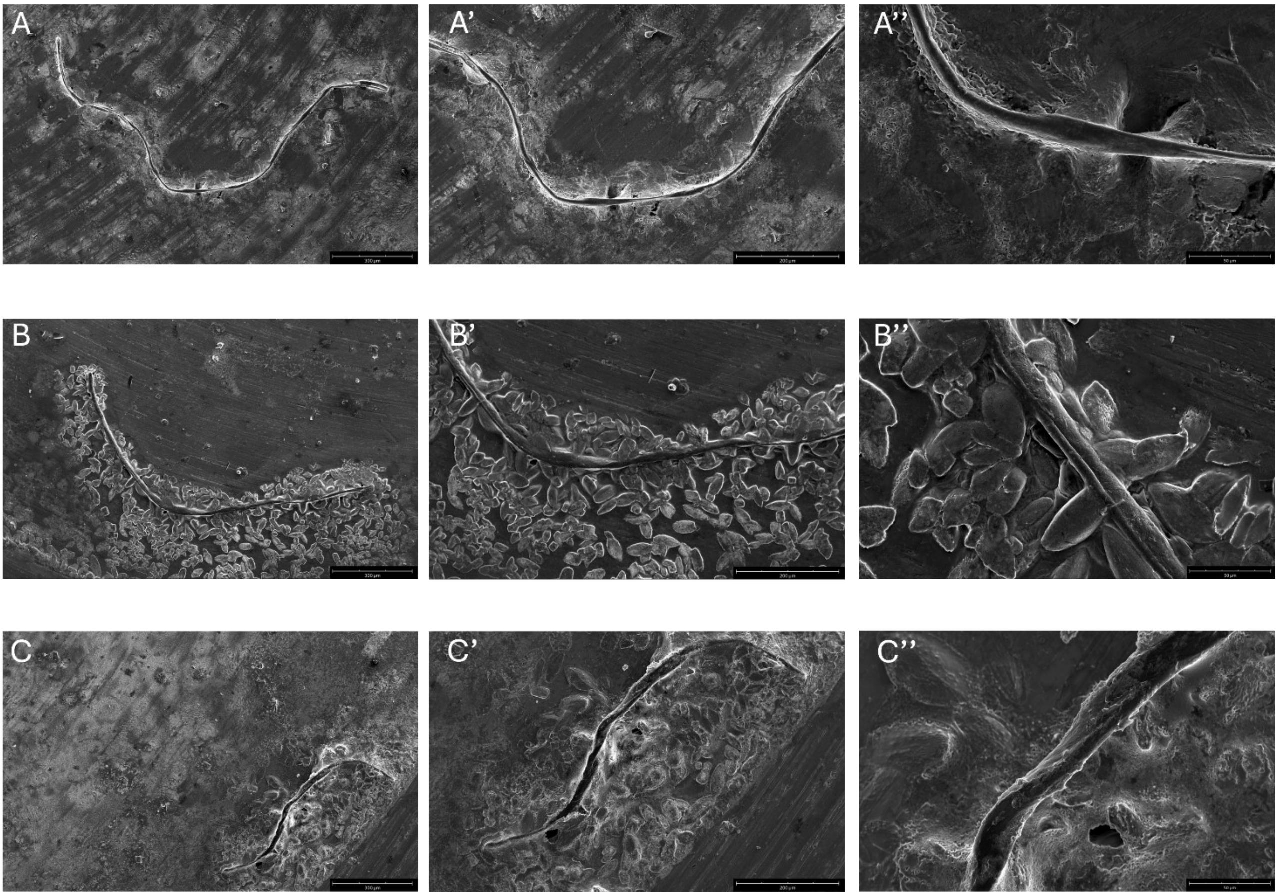

Figure S7. Scanning electron microscopy of A$\beta_{1\text{-}42}$ alone at a magnification of 330x (300 µm scale bar, A, B, C), 790x (200 µm scale bar, A′, B′, C′) and 2500x (50 µm scale bar, A′′, B′′, C′′). These data represent three of the four independent experiments performed.

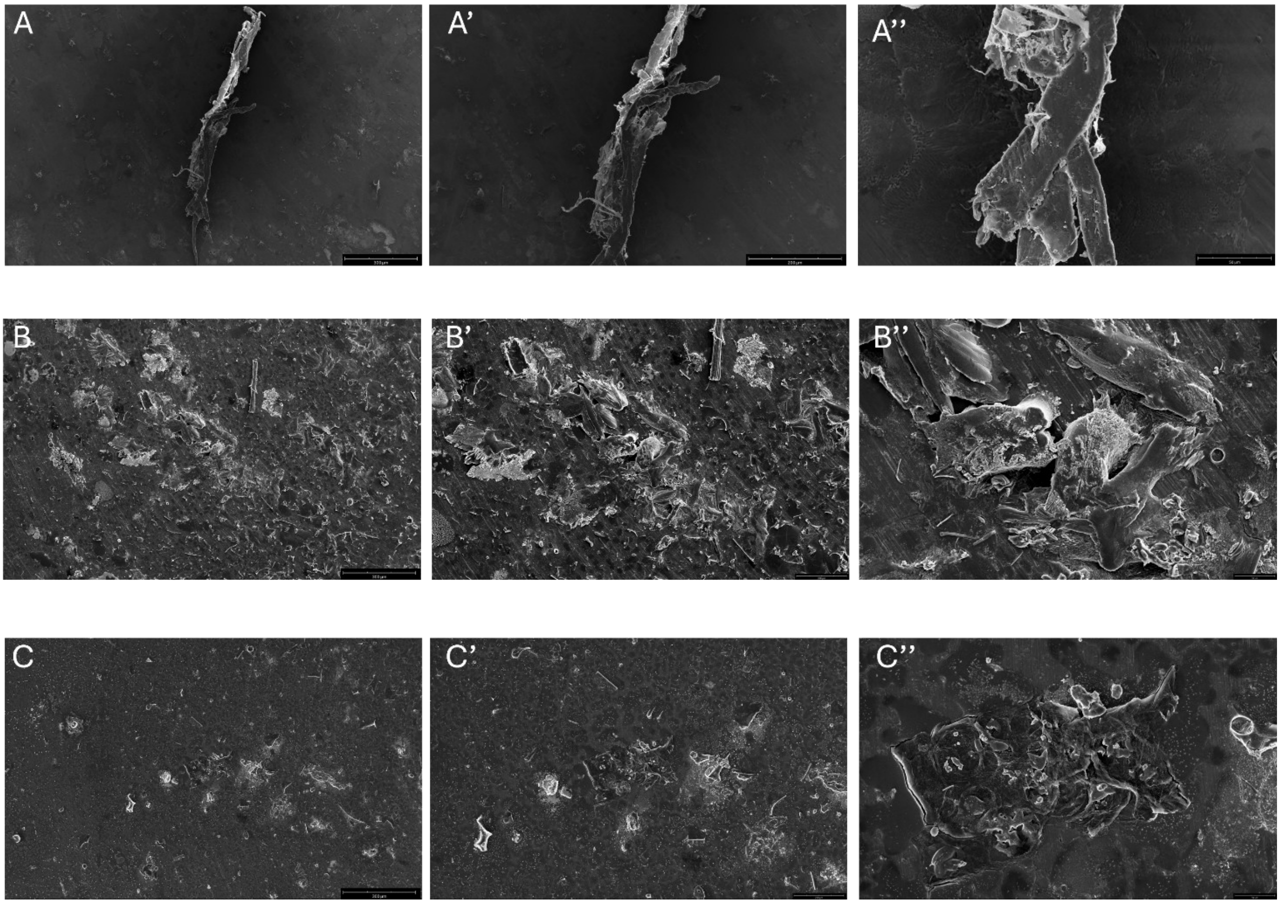

Figure S8. Scanning electron microscopy of Aβ_{1-42} in the presence of **Pt-Ac-rhein** at a magnification of 330x (300 µm scale bar, A, B, C), 790x (200 µm scale bar, A', B', C') and 2500x (50 µm scale bar, A'', B'', C''). These data represent three of the four independent experiments performed.

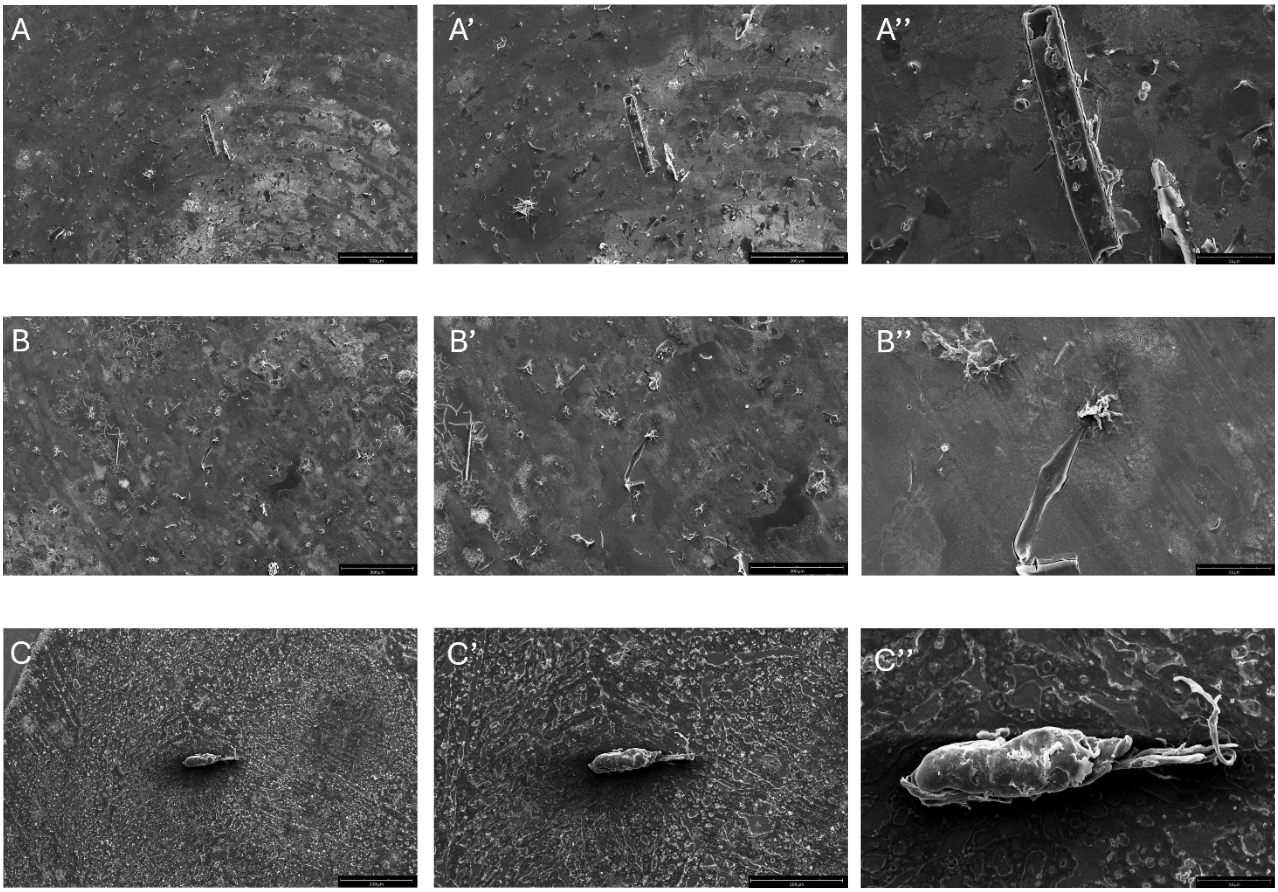

Figure S9. Scanning electron microscopy of A$\beta_{1\text{-}42}$ in the presence of rhein at a magnification of 330x (300 µm scale bar, A, B, C), 790x (200 µm scale bar, A', B', C') and 2500x (50 µm scale bar, A'', B'', C''). These data represent three of the four independent experiments performed.

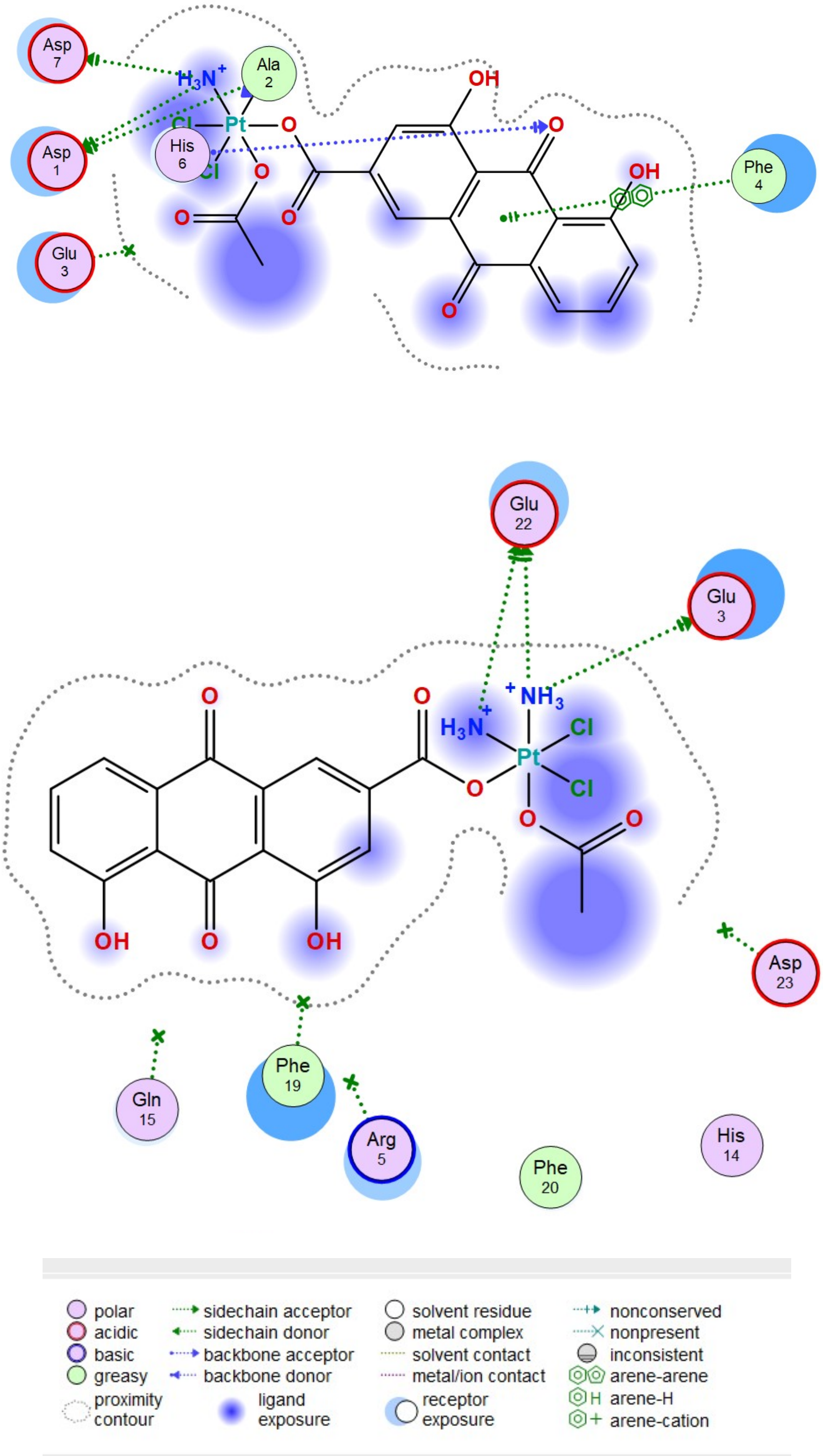

Figure S10. Ligand interactions for best docked complex of Pt-Ac-Rhein with Aβ $_{1\text{-}42}$ monomer and tetramer.

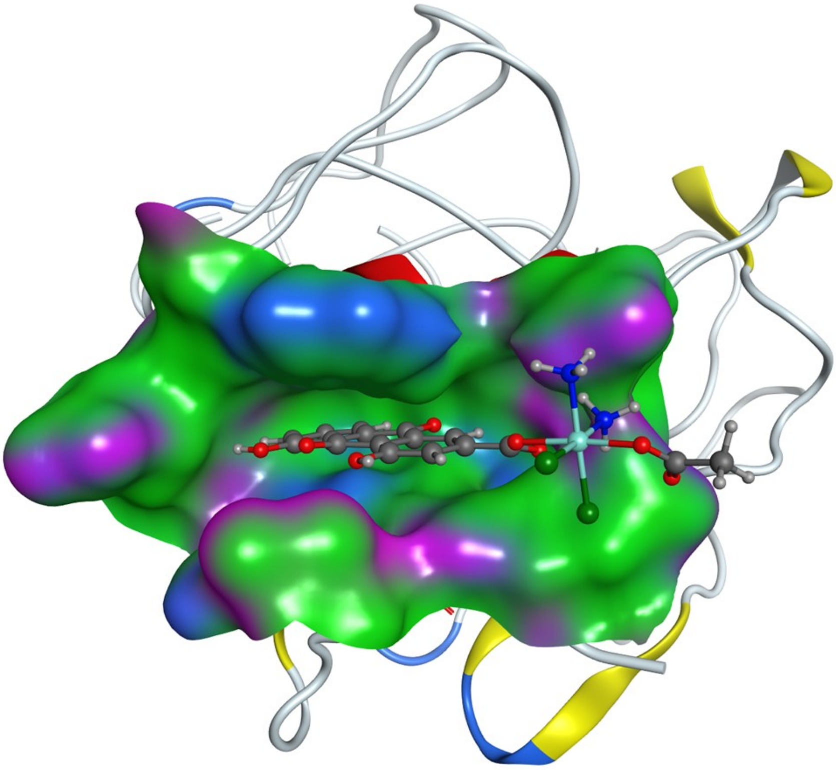

Figure S11. Best docked pose of **Pt-Ac-rhein** with Aβ_{1-42} tetramer. **Pt-Ac-rhein** is shown as ball-and-stick, receptor is shown as a surface coloured by lipophilicity: green represents lipophilic areas, pink potential hydrogen bonding sites, and blue polar regions.

Table S1: Table of main observed ions relative to the species formed by the Aβ_{1-42} alone and mixed with **Pt-Ac-rhein**. Experimental and theoretical mass and charge were reported for each adduct.

	Description	m/z (charge)		Theoretical m/z
		Peptide	+metal complex	
Aβ_{1-42}: **Pt-Ac-rhein**	Aβ_{1-42}	1505.28 (+3) 1129.42 (+4) 903.96 (+5) 753.44 (+6)	1505.29 (+3) 1129.77 (+4) 903.95 (+5) 753.43 (+6)	1505.71 1129.54 903.83 753.36
	Aβ_{1-42} + **Pt-Ac-rhein**	-	1719.12 (+3) 1290.76 (+4)	1719.71 1290.03

Table S2: Docking ChemPLP scores for **Pt-Ac-rhein**, rhein and **Pt-Ac-OH** with Aβ_{1-42} monomer and tetramer

	Pt-Ac-rhein	**rhein**	**Pt-Ac-OH**
Monomer 1	-78.0	-72.7	-51.8
Monomer 2	-83.4	-66.5	-62.1
Monomer 3	-86.3	-69.0	-64.1
Monomer 4	-79.3	-73.4	-57.8
Monomer 5	-76.2	-67.0	-54.7
Monomer 6	-75.5	-69.3	-53.6
Monomer 7	-80.0	-89.0	-56.9
Monomer 8	-106.8	-62.7	-57.1
Monomer 9	-79.7	-67.2	-60.1
Monomer 10	-79.3	-80.3	-51.5
Mean monomer	-82.5	-71.7	-57.0
Tetramer 1	-91.4	-72.1	-60.6
Tetramer 2	-81.0	-75.8	-63.1
Tetramer 3	-78.4	-75.5	-60.6

Tetramer 4	-102.4	-93.9	-60.3
Tetramer 5	-78.5	-65.4	-57.4
Mean tetramer	-86.3	-76.5	-60.4