Supplementary materials

Exosomes loaded with ultrasmall Pt nanoparticles: A novel low-toxicity alternative to cisplatin

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GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
Control	100 μg Pt-Exos$^{U251\text{-}MG}$	100 μg Pt-Exos$^{U251\text{-}MG}$	Cisplatin	Cisplatin
-	IV	IT	IV	IT

Table S1. Experimental groups included in the *in vivo* study.

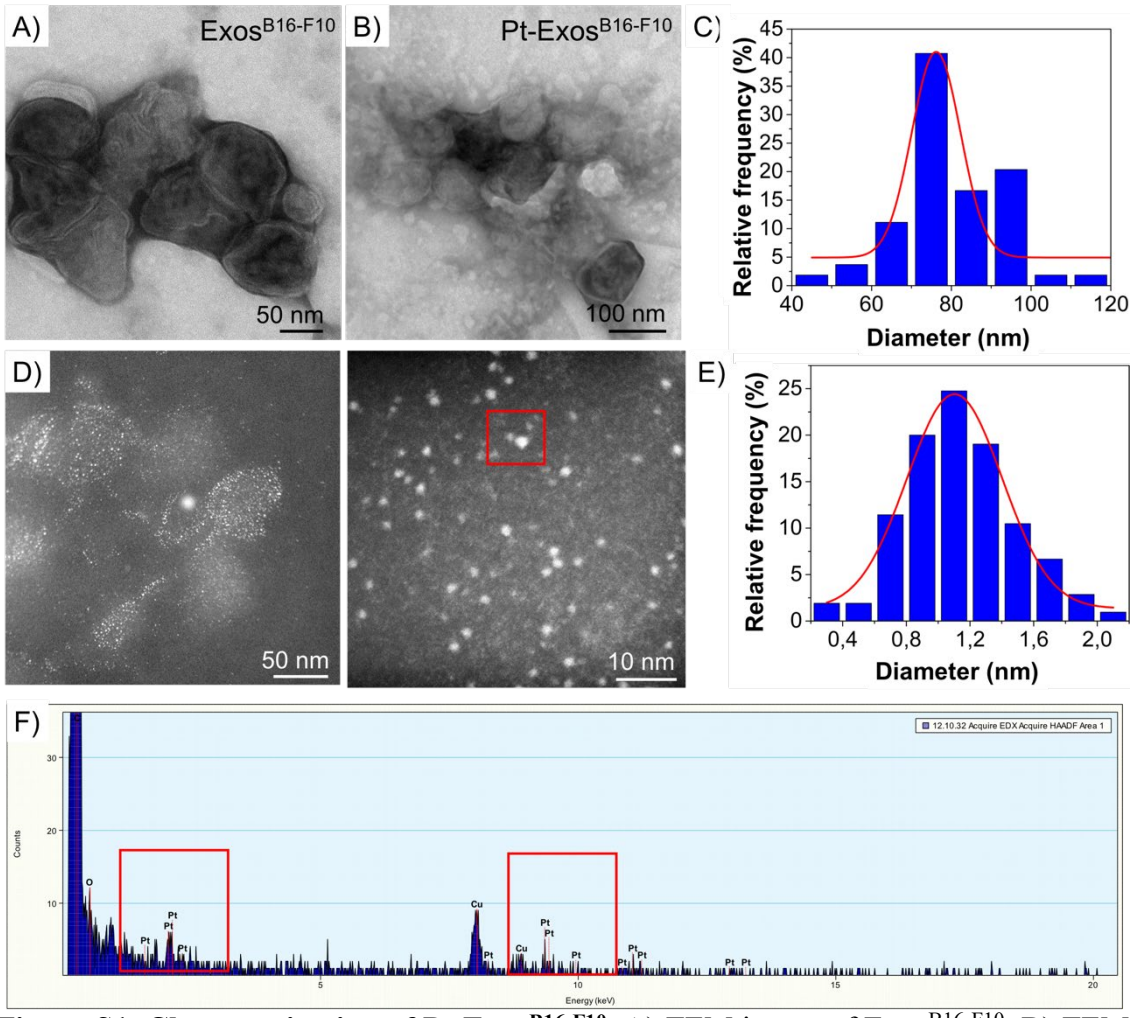

Figure S1. **Characterization of Pt-Exos$^{B16\text{-}F10}$**. A) TEM image of Exos$^{B16\text{-}F10}$. B) TEM image of Pt-Exos$^{B16\text{-}F10}$. C) Size distribution histogram of Pt-Exos$^{B16\text{-}F10}$ diameter. D) HAADF-STEM images of Pt-Exos$^{B16\text{-}F10}$. E) Size distribution histogram of PtNPs generated within exosomes. F) EDX analysis of the PtNPs synthesized inside the Exos$^{B16\text{-}F10}$.

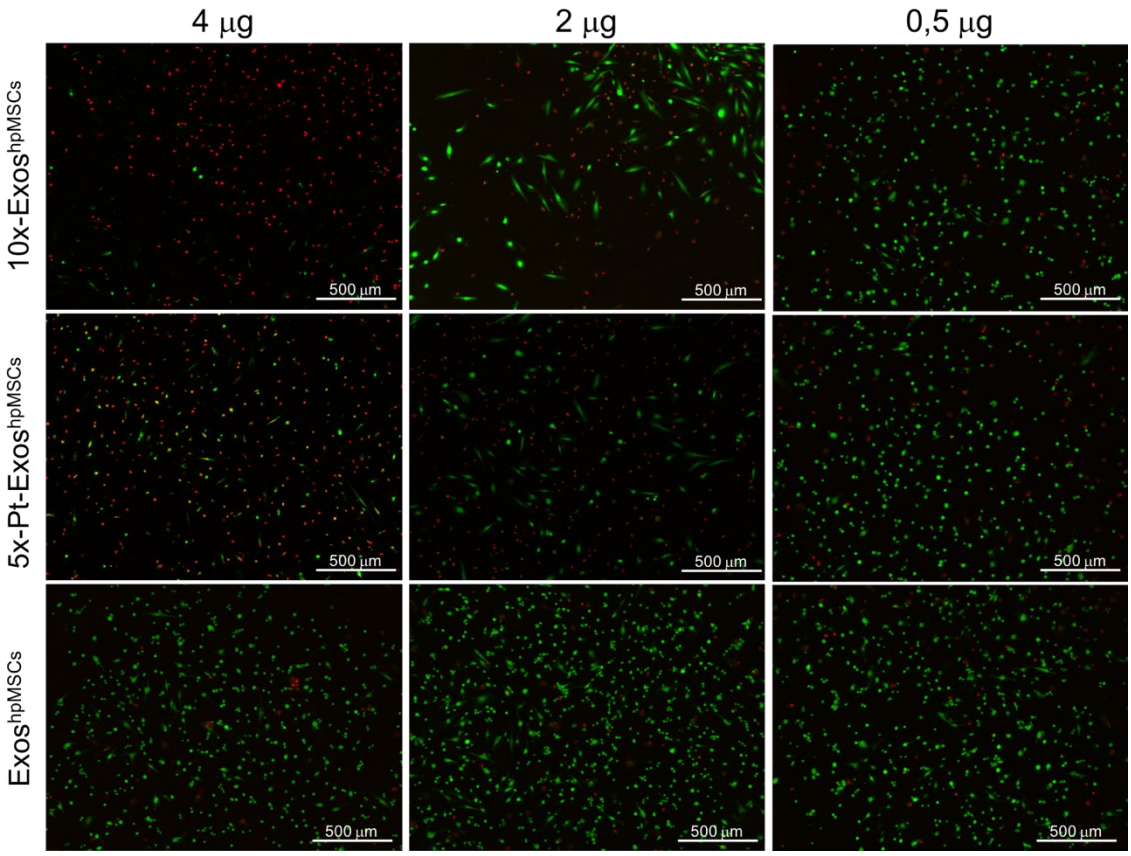

Figure S2. **LIVE/DEAD assay**. Influence of the concentration of Pt-loaded exosomes on cell viability after 48 h of incubation with the corresponding parental cells.

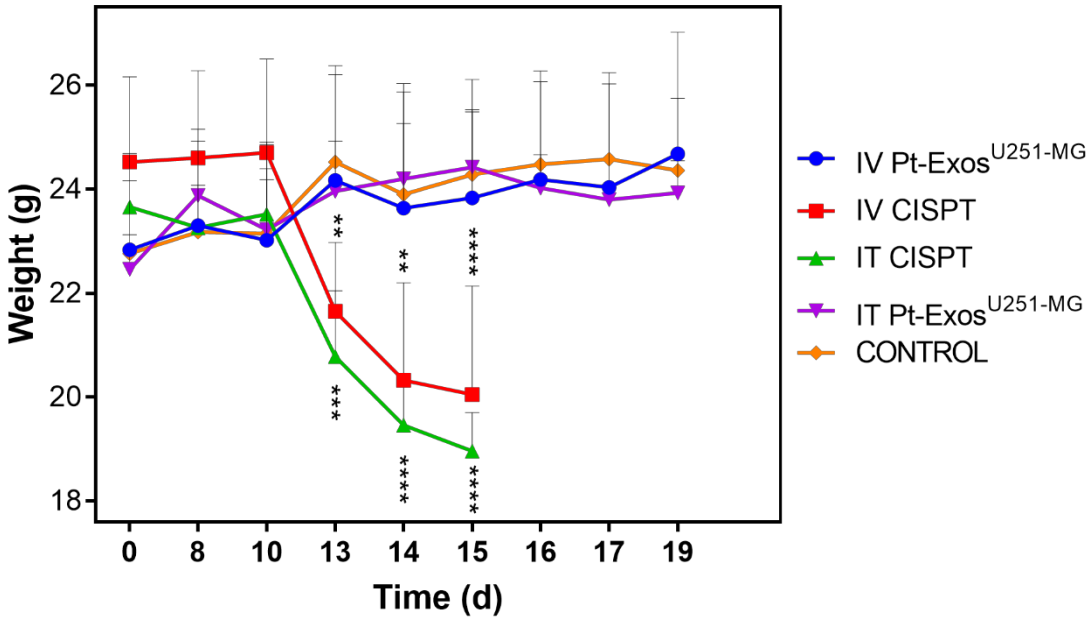

Figure S3. Weight evolution of mice upon cisplatin and Pt-Exos treatment.

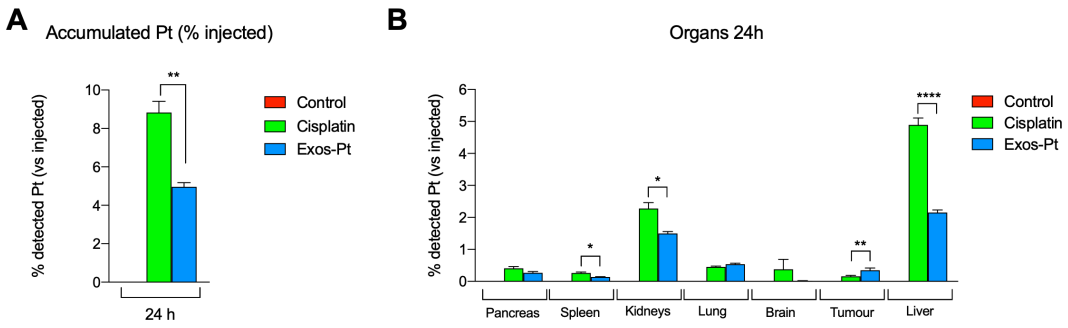

Fig. S4. **Biodistribution of Pt 24 h after IV injection of cisplatin and Pt-Exos$^{U251-MG}$. (A)** Amount of detected Pt as a percentage of the total injected per animal (sum of the Pt mass detected in every organ as a percentage of the mass injected) 24 h after treatment. **(B)** Biodistribution of Pt after 24 h in analyzed organs: pancreas, spleen, kidneys, liver, lung, brain and tumor as percentage of the total amount of injected Pt.

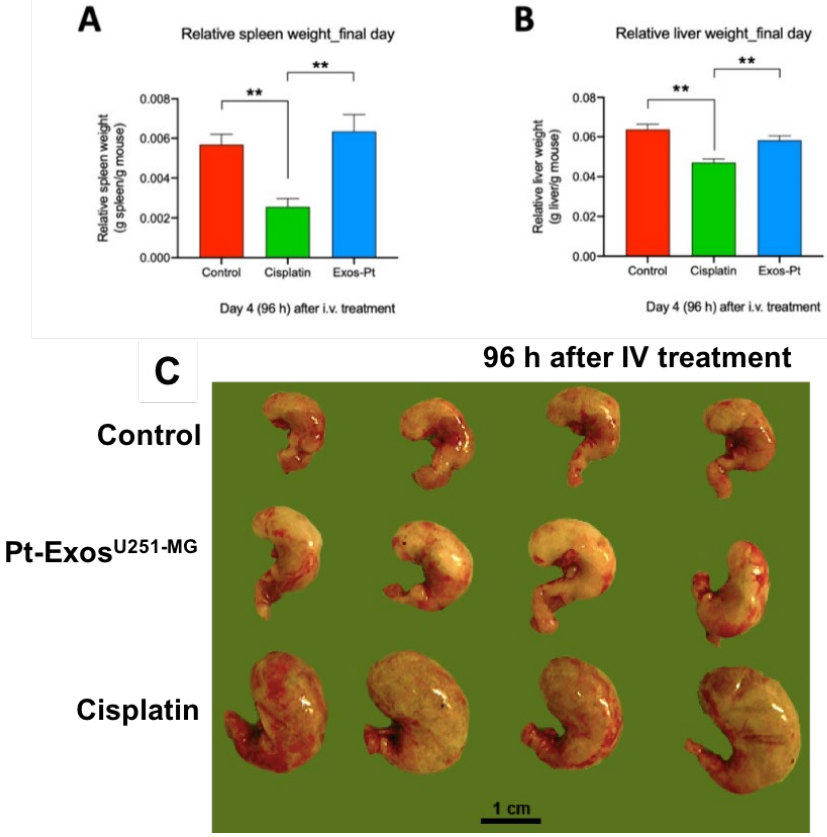

Figure S5. Organic alterations 96 hours after cisplatin intravenous treatment: (A) Reduction of relative spleen weight, (B) Reduction of relative liver weight, (C) enlargement of stomach.

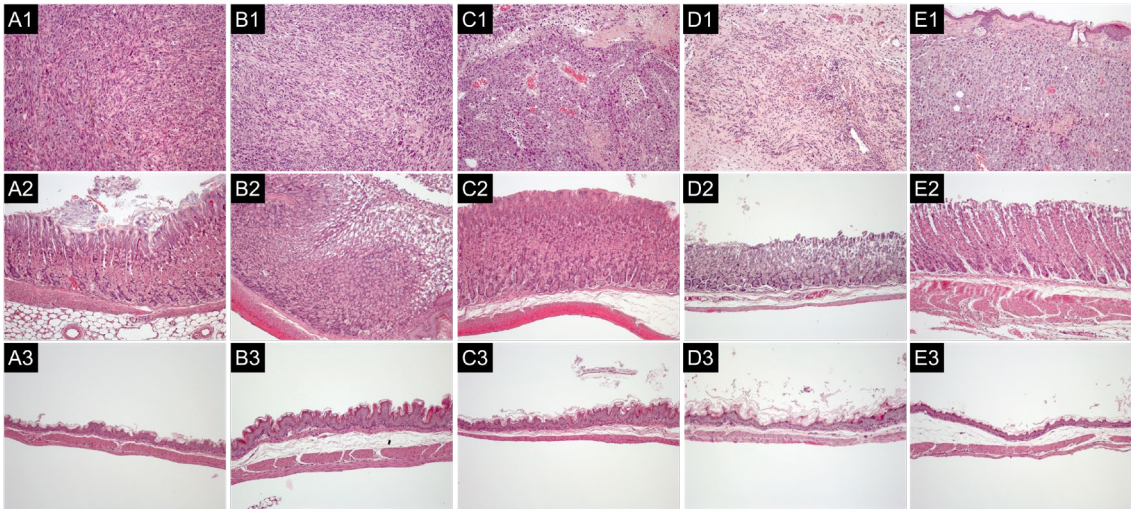

Figure S6. H-E analysis. Tumor (A1), glandular stomach (A2) and non-glandular stomach (A3) from control group. Tumor (B1), glandular stomach (B2) and non-glandular stomach (B3) from IV Pt-Exos treated group. Tumor (C1), glandular stomach (C2) and non-glandular stomach (C3) from IT Pt-Exos treated group. Tumor (D1), glandular stomach (D2) and non-glandular stomach (D3) from IV cisplatin treated group. Tumor (E1), glandular stomach (E2) and non-glandular stomach (E3) from IT cisplatin treated group.