



Supplementary Materials

Transferrin-decorated PLGA nanoparticles loaded with an organoselenium compound as an innovative approach to sensitize MDR tumor cells: an *in vitro* study using 2D and 3D cell models

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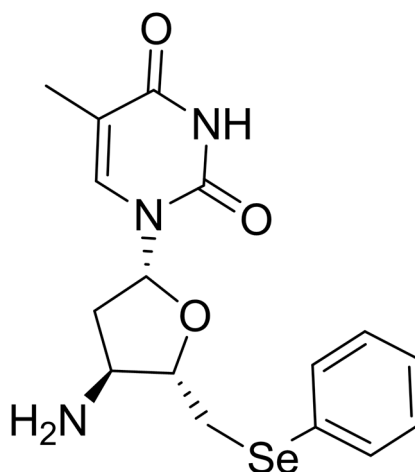


Figure S1. Chemical structure of 5'-Se-(phenyl)-3-(amino)-thymidine.

Table S1. Characterization of Tf-ACAT-Se-PLGA-NPs.

	Tf-ACAT-Se-PLGA-NPs			Mean	SD
Particulatesize (nm)	121.3	148.1	142.1	137	5.48
PDI	0.128	0.103	0.151	0.127	0.02
ZP (mV)	-4.17	-3.64	-5.28	-4.36	0.82
pH	7.52	7.6	7.03	7.38	0.29

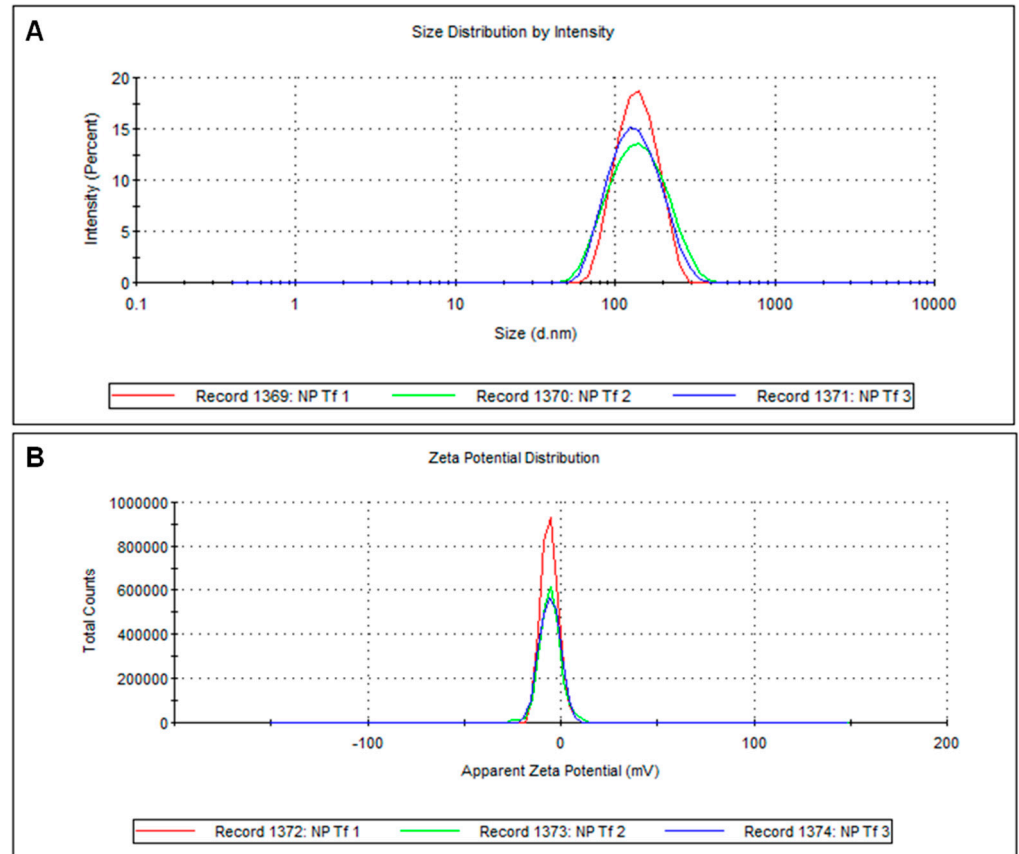


Figure S2. Characterization of Tf-ACAT-Se-PLGA-NPs determined by dynamic light scattering. Size distribution (A) and zeta potential (B).

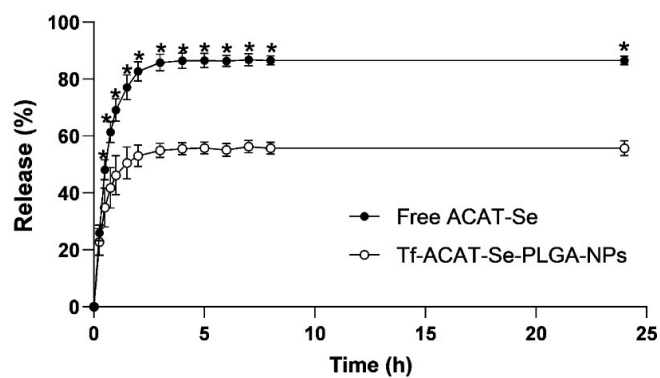


Figure S3. *In vitro* cumulative ACAT-Se release. Statistical analyses were performed using ANOVA followed by Tukey's multiple comparison test. *Significant difference from Tf-ACAT-Se-PLGA-NPs ($p < 0.05$).

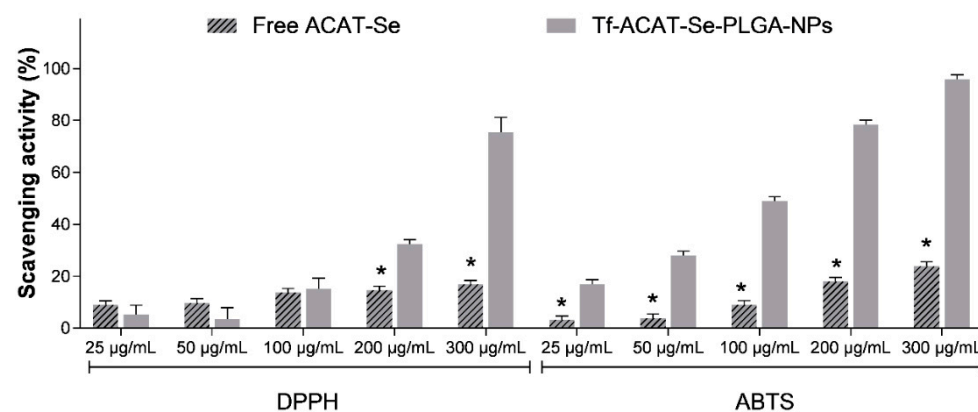


Figure S4. Scavenging activity of free ACAT-Se and Tf-ACAT-Se-PLGA-NPs by DPPH and ABTS assays. Results are expressed as mean \pm SD of three independent experiments. Statistical analyses were performed using ANOVA followed by Student-Newman-Keuls multiple comparison test. *Significant difference from Tf-ACAT-Se-PLGA-NPs ($p < 0.05$).

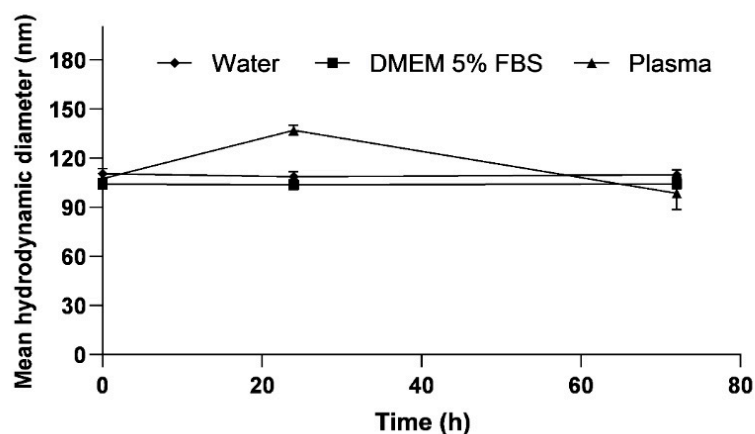


Figure S5. Mean hydrodynamic diameter of Tf-ACAT-Se-PLGA-NPs after incubation with water, DMEM 5% FBS (Dulbecco's Modified Eagle's Medium with 5% fetal bovine serum) and plasma up to 72 h. Each value represents mean \pm SD. Statistical analyses were performed by Student t-test and no significant differences were found.

Table S2. IC₅₀ values (µg/mL) after 72 h of treatment

	IC ₅₀				
	A375	HeLa	MCF-7	U-87	NCI/ADR-RES
Free ACAT-Se	NC	72.82*	97.38*	NC	NC
ACAT-Se-PLGA-NPs	49.56	82.57*	32.55	52.86	143.45*
Tf-ACAT-Se-PLGA-NPs	3.53	11.52	6.24	11.72	23.73

NC – not calculated, could not be determined due the low cytotoxicity.

*Estimated IC₅₀ based on dose-response curves.

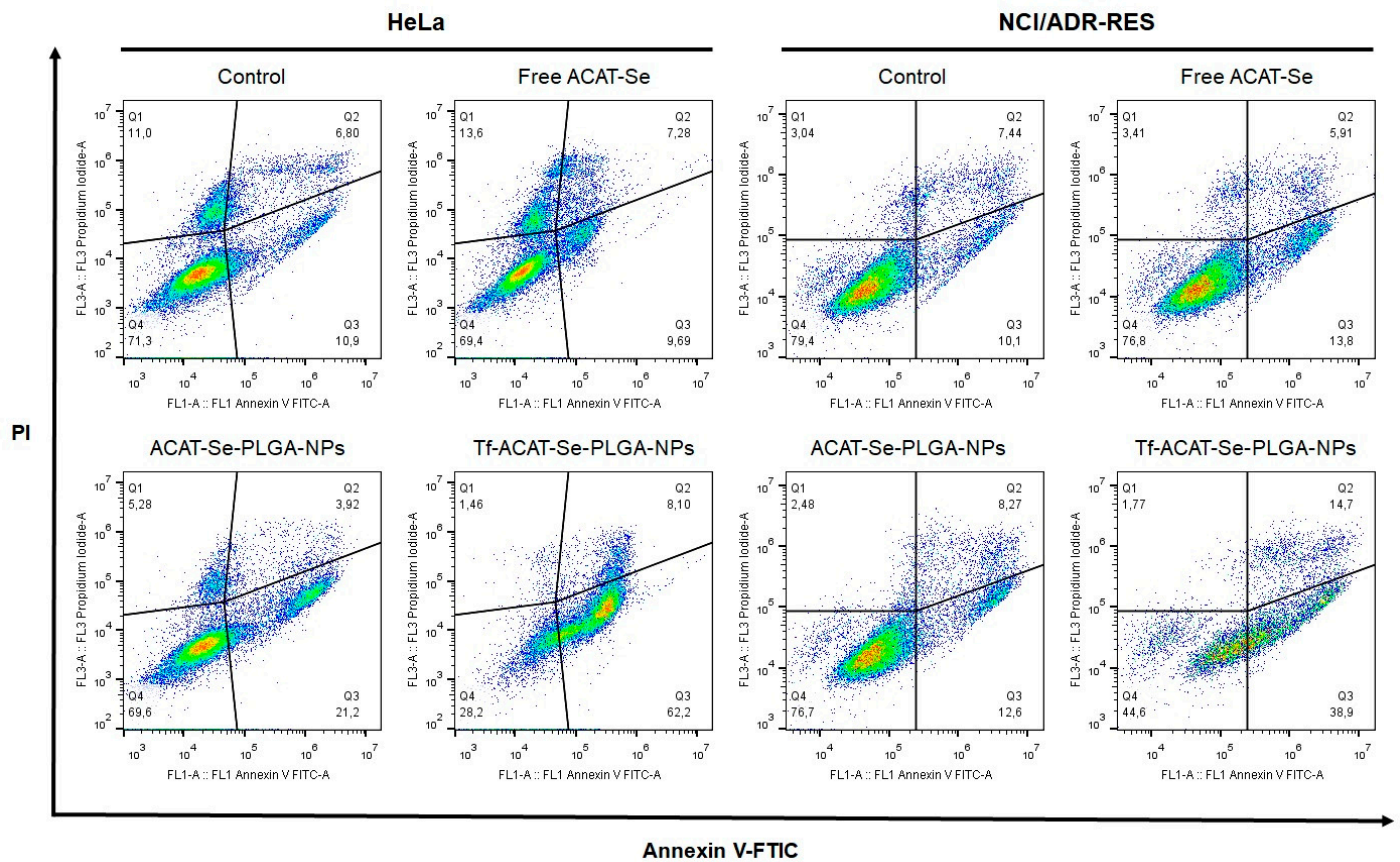


Figure S6. Scatter plots for HeLa and NCI/ADR-RES cells after 24 h incubation with free ACAT-Se, ACAT-Se-PLGA-NPs or Tf-ACAT-Se-PLGA-NPs. The results were obtained through flow cytometry after Annexin V-FITC/PI staining.

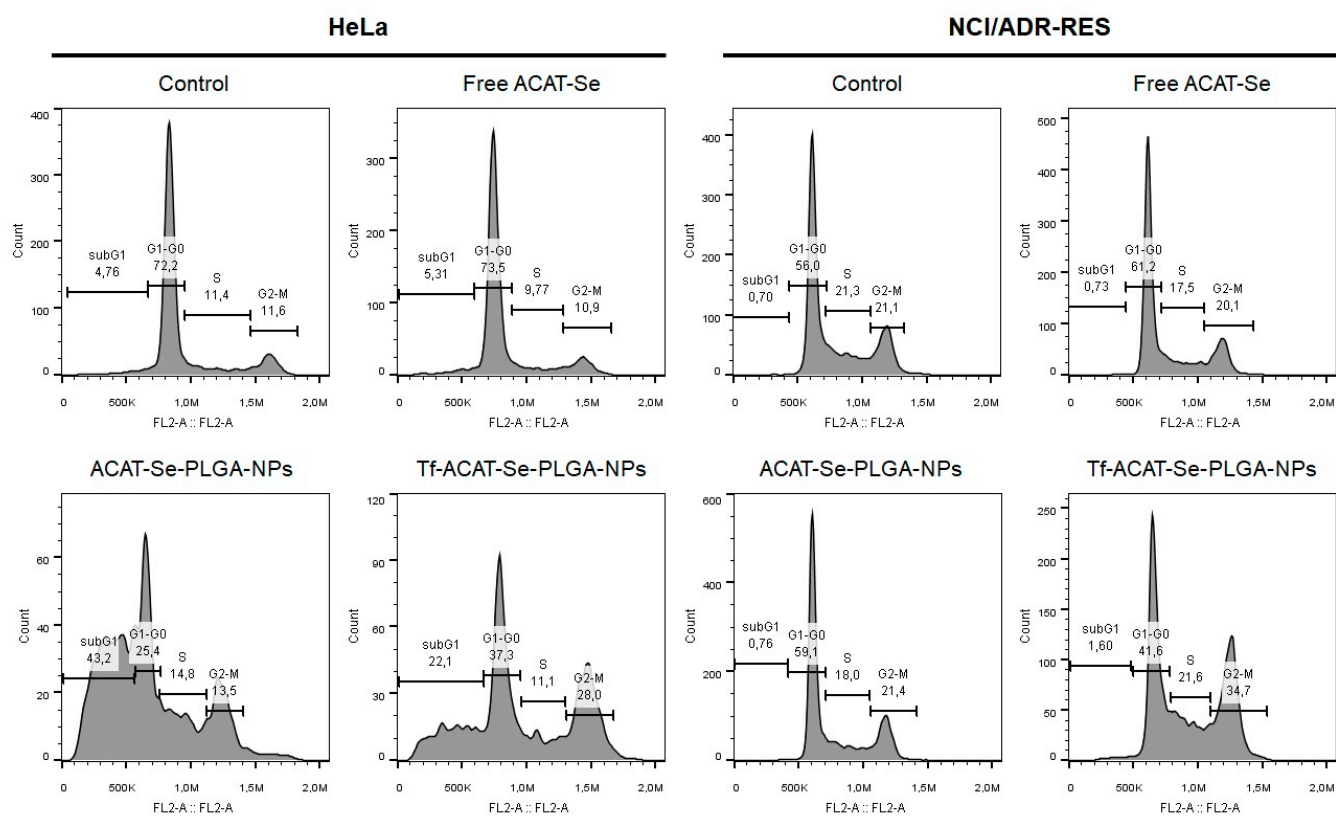


Figure S7. Histogram plots of HeLa and NCI/ADR-RES cells distribution in the different phases of the cell cycle after 24 h incubation with free ACAT-Se, ACAT-Se-PLGA-NPs or Tf-ACAT-Se-PLGA-NPs.