Electronic Supplementary Information

for

Liposomes Loaded with Polyphenol-Rich Grape Pomace Extracts Protect from Neurodegeneration in a Rotenone-Based *in Vitro* Model of Parkinson's Disease

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Author Contributions

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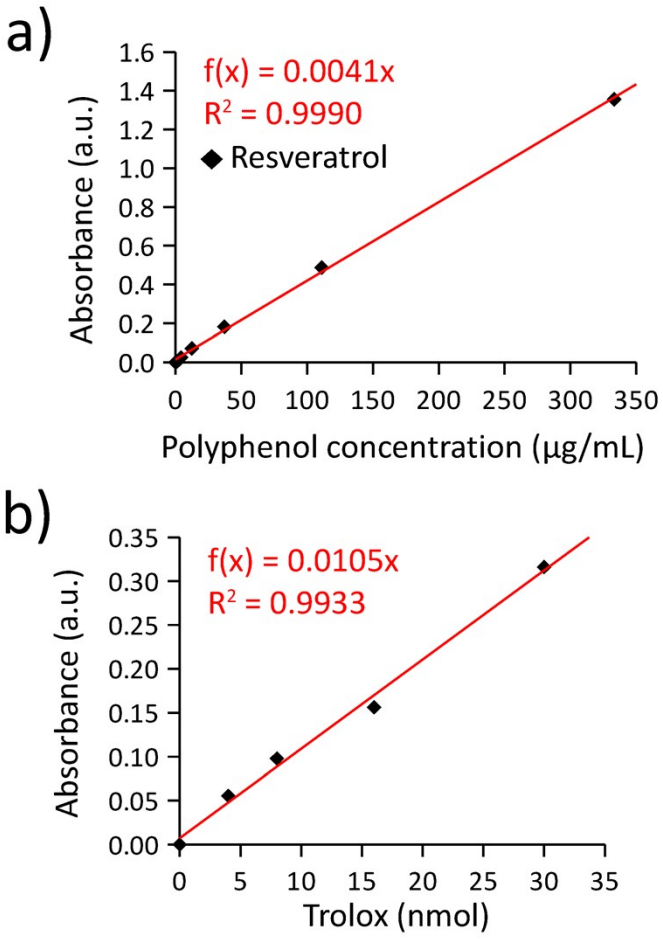

Figure S1. a) Folin-Ciocalteu assay calibration curve for resveratrol at different concentrations (0.00, 1.37, 4.12, 12.35, 37.04, 111.11, and 333.33 µg/ml). b) Antioxidant capacity evaluation calibration curve for 0, 4, 8, 16, and 30 nmol of trolox.

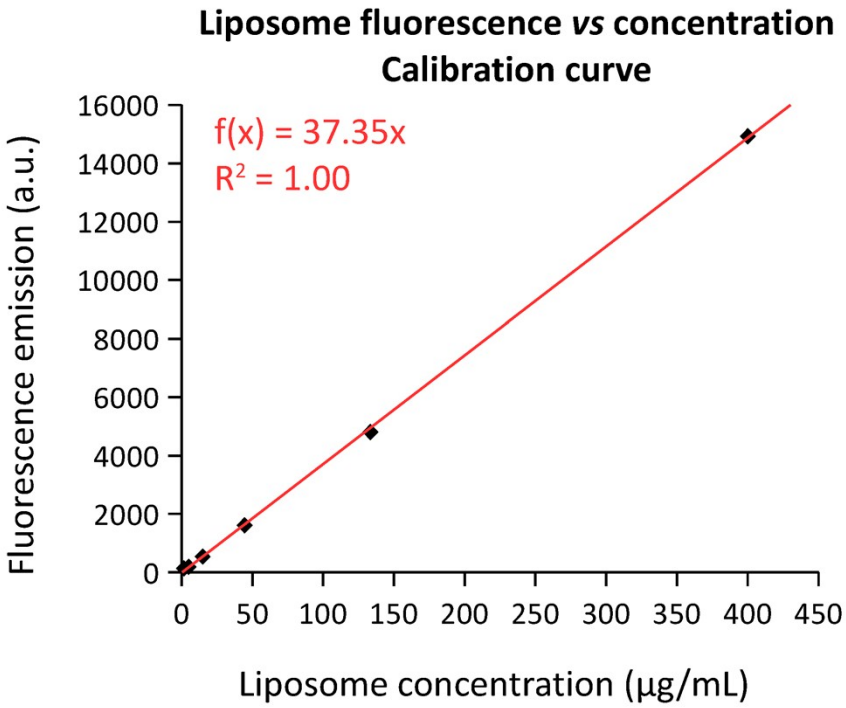

Figure S2. Calibration curve for ext-LS quantification, performed with 1.65, 4.49, 14.81, 44.44, 133.33, and 400 µg/ml DiO-stained ext-LSs.

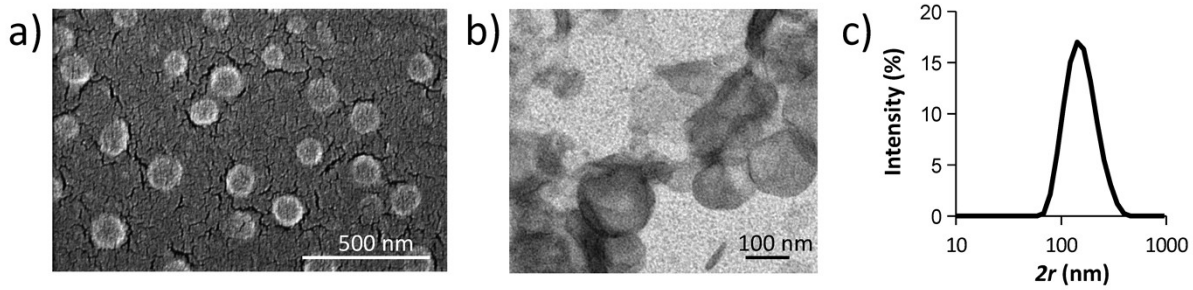

Figure S3. a) Representative scanning electron microscopy (SEM) image, b) transmission electron microscopy image and c) hydrodynamic size (*2r*) of empty liposomes.

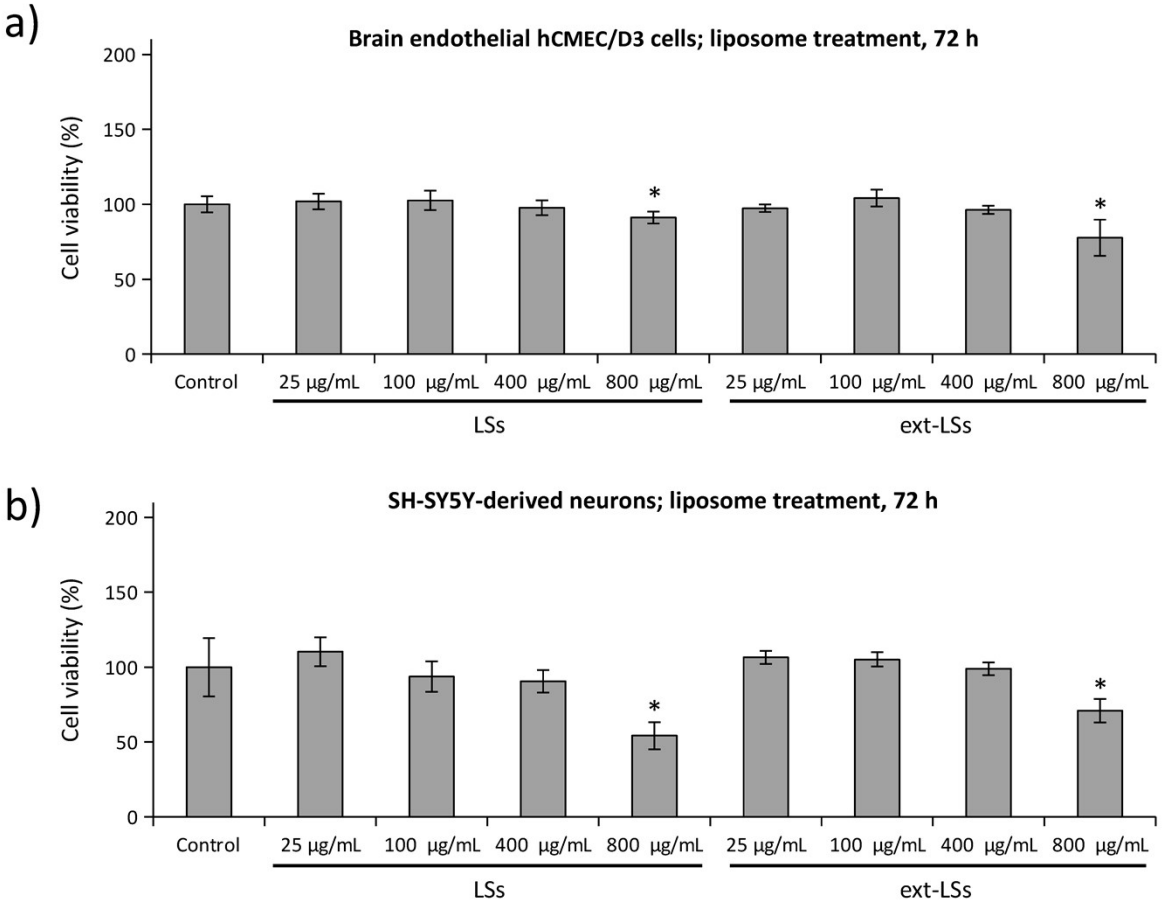

Figure S4. WST-1 cell viability assay for a) brain endothelial hCMEC/D3 cells and b) SH-SY5Y-derived neurons treated for 72 h with non-loaded LSs or ext-LSs (0, 25, 100, 400, or 800 µg/ml concentrations). *$p < 0.05$.

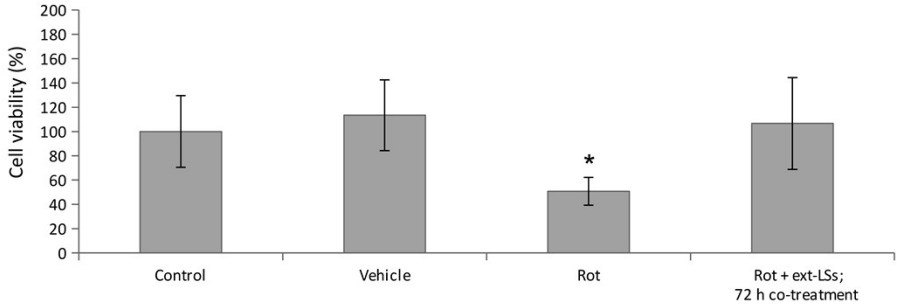

Figure S5. WST-1 cell viability assay of SH-SY5Y-derived neurons treated with rot (1.00 μM) for 72 h ("Rot)", or with combined 1.00 μM rot + ext-LS for 72 h ("Rot + ext-LSs; 72 h co-treatment"). The vehicle is DMSO (1:1000). *$p < 0.05$.

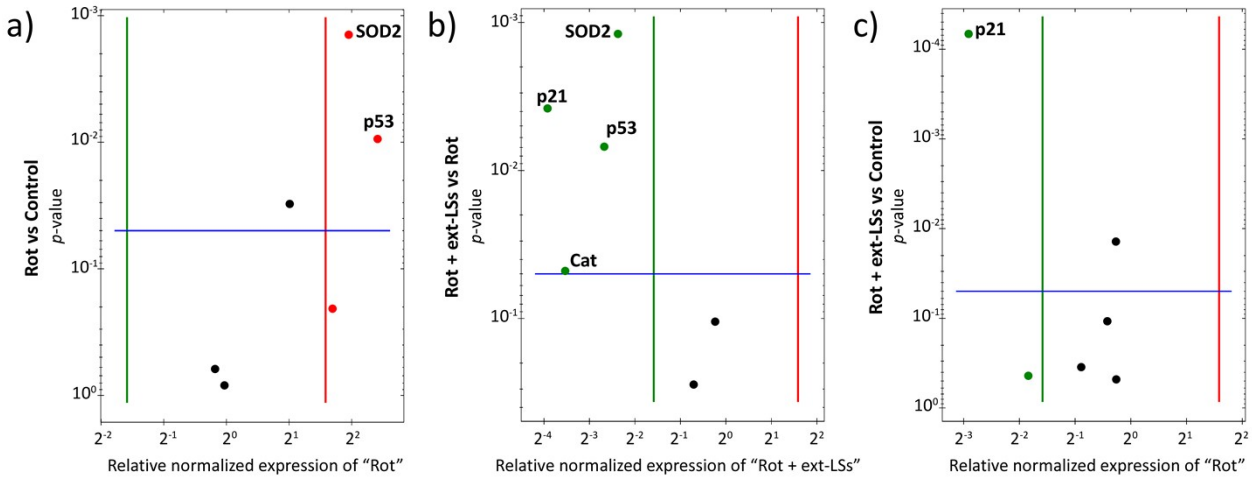

Figure S6. Volcano plot showing the *p*-value versus the fold change in qRT-PCR analysis for a) "Rot" *vs.* "Control", b) "Rot + ext-LSs" *vs.* "Rot", and c) "Rot + ext-LSs" *vs.* "Control".

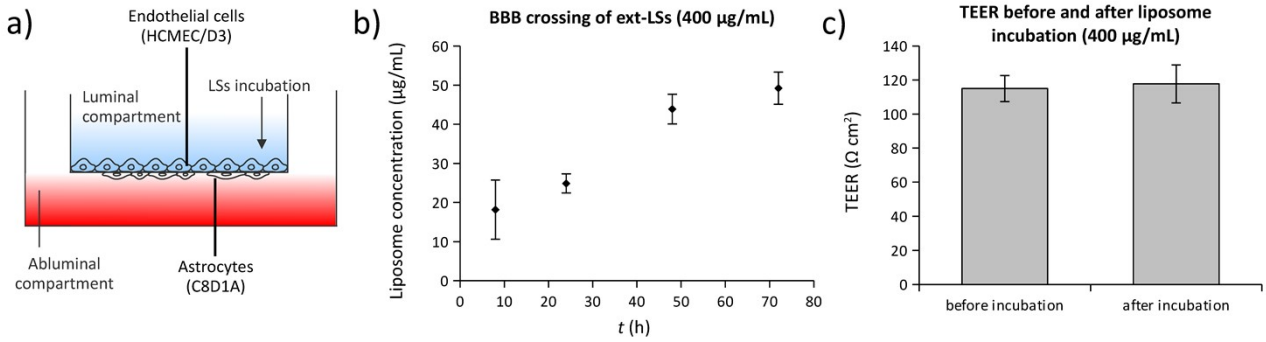

Figure S7. BBB crossing of the ext-LSs investigated on a multicellular *in vitro* model. a) Schematic representation of the *in vitro* BBB system with luminal (in blue) and abluminal (in red) compartments separated by astrocytes and by an endothelial cell layer; b) ext-LS concentration detected in the abluminal compartment at different time points (0, 8, 24, 48, 72 h) after incubating the luminal compartment with 400 µg/ml DiO-stained ext-LSs; c) Transendothelial electrical resistance (TEER) measured before and after ext-LS incubation.

Table S1. Sequence of the forward (F) and reverse (R) primers used for the qRT-PCR.

Gene	Primer sequence
Cat_F	5’-TGAACTGTCCCTACCGTGCT-3’
Cat_R	5’-GGAGCACCACCCTGATTGTC-3’
GSS_F	5’-GACCAAGACCGAAGGCTGTT-3’
GSS_R	5’-AGACGTGCTTCCCAATTCTGTA-3’
Hprt1_F	5’-AGATGGTCAAGGTCGCAAG-3’
Hprt1_R	5’-GTATTCATTATAGTCAAGGGCATACT-3’
Rpl32_F	5’-GAGCGATCTCGGCACAGTA-3’
Rpl32_R	5’-GAAGTTCCTGGTCCACAACG-3’
SOD1_F	5’-GCACACTGGTGGTCCATGAAA-3’
SOD1_R	5’-ACACCACAAGCCAAACGACT-3’
SOD2_F	5’-GAACCCAAAGGGGAGTTGCT-3’
SOD2_R	5’-AGCCTTGGACACCAACAGAT-3’
p53_F	5'-GGGACGGAACAGCTTTGAGG-3'
p53_R	5'-GTTGGGCAGTGCTCGCTTAG-3'
p21_F	5'-GGATGAGTTGGGAGGAGGCA-3'
p21_R	5'-GTGGTAGAAATCTGTCATGCTGGT-3'