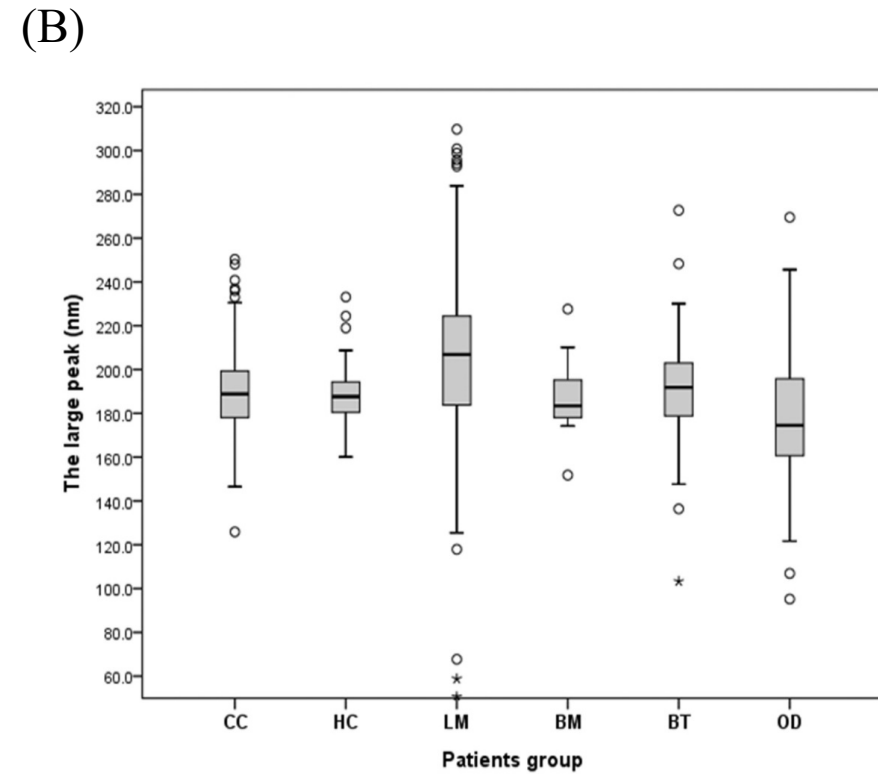
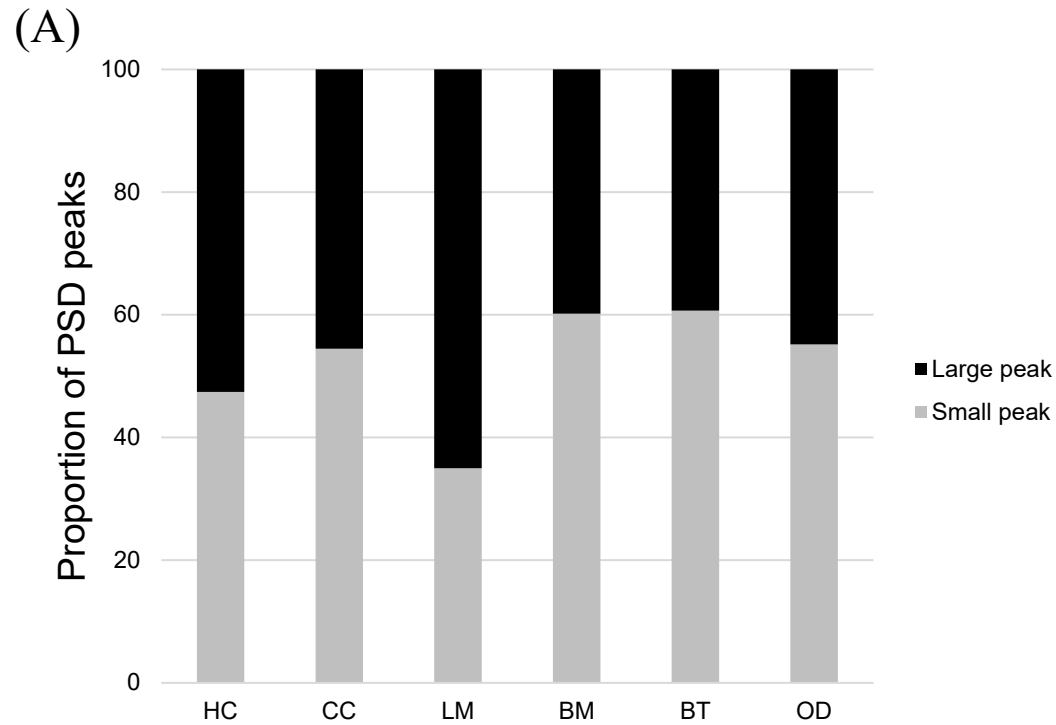
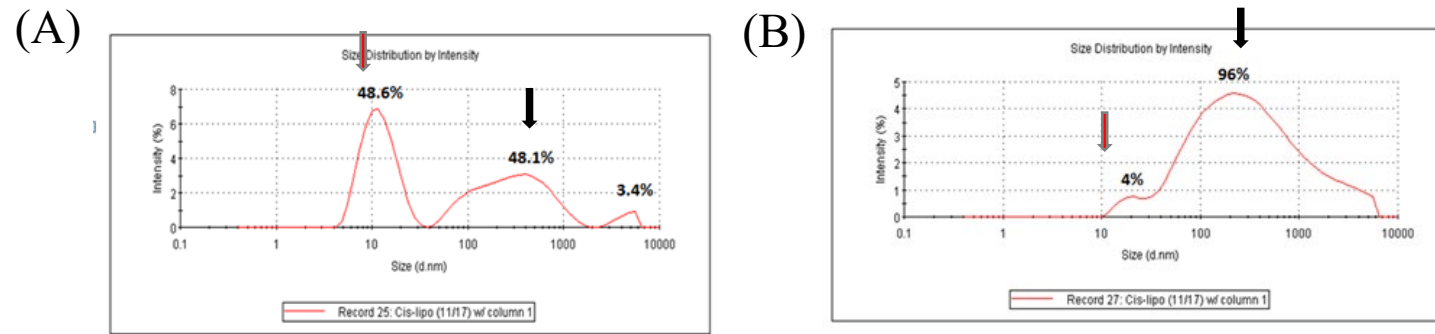


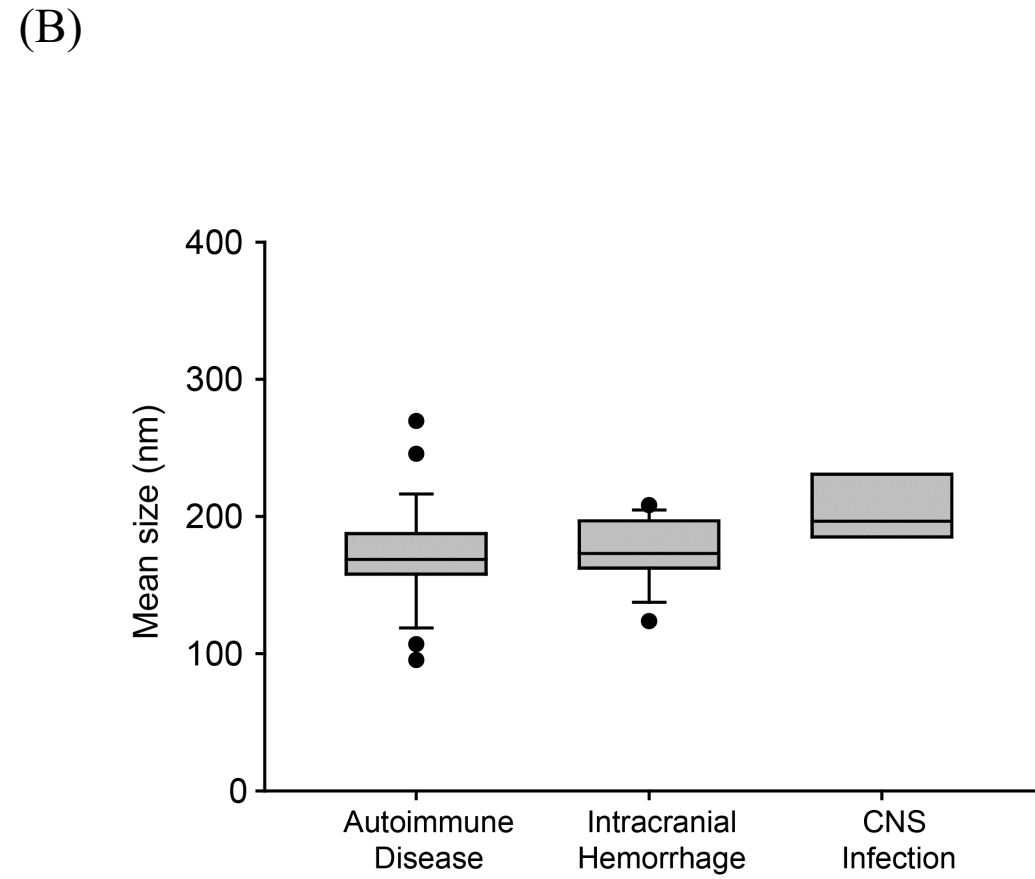
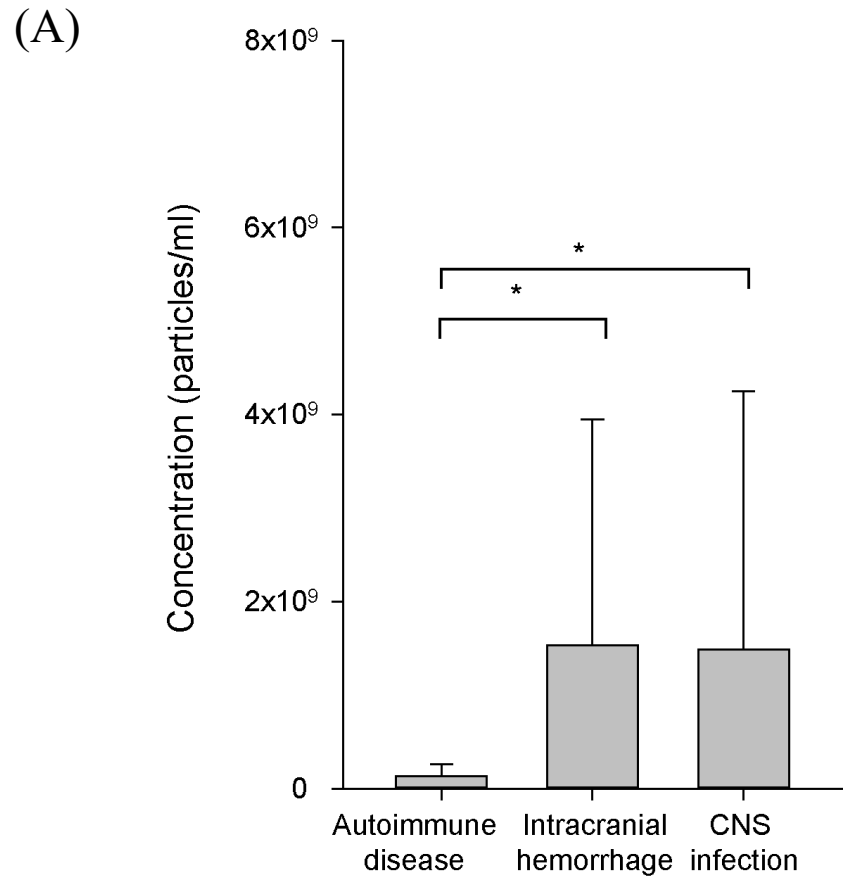
Supplementary figure 1. Preliminary analysis of extracellular nanoparticles in CSF. (A) NTA-measured nanoparticle concentration changes according to different storage temperature before cell-down. (B) DLS-measured change of peaks at nano-range in cerebrospinal fluid of pre-treatment (upper) and post-treatment (lower) from a patient who received wholebrain radiation therapy.



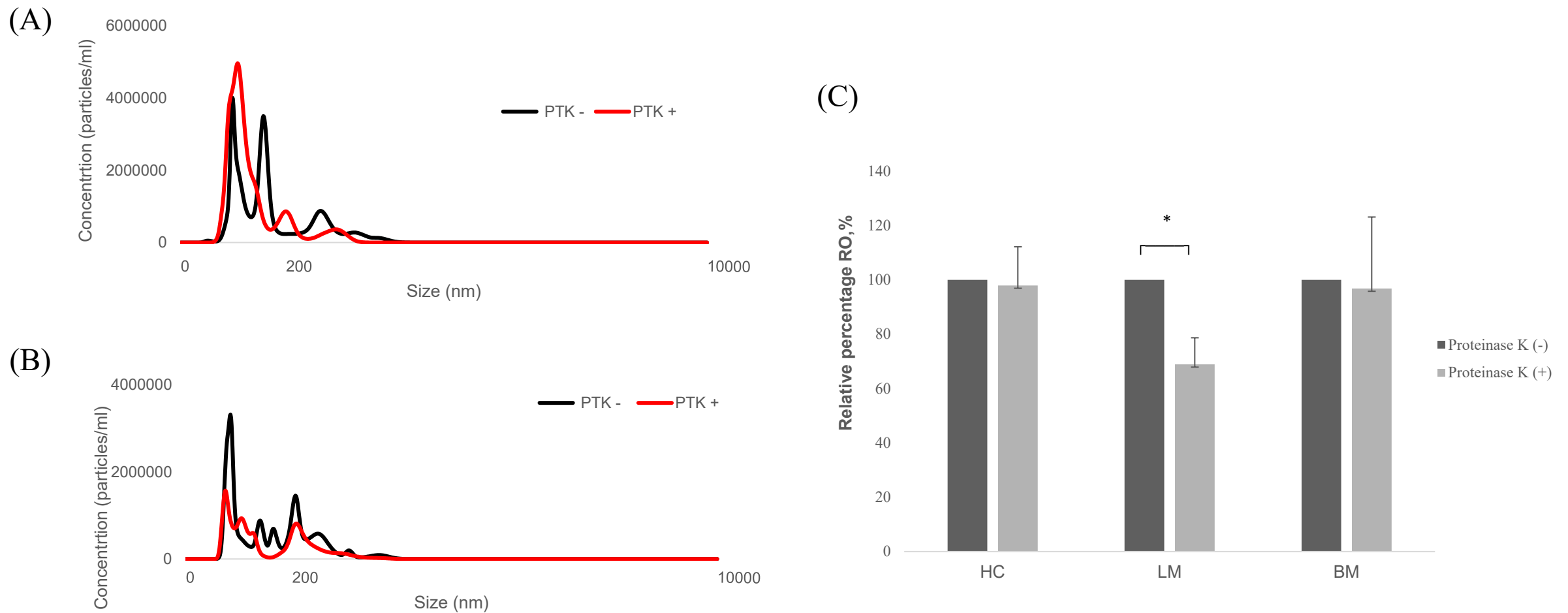
Supplementary figure 2. The different distribution of intensity peaks in Dynamic Light Scattering (DLS) analysis (A) The proportion of observed two peaks according to patients' group. Leptomeningeal metastasis (LM) showed significantly lower small peak proportion and higher large peak proportion than other groups (*Student t-test*, $p < 0.001$). (B) Box plots representing the size of large peak according to patients' group. LM groups showed significantly larger size than other groups. Thick line is mean value and the box range represents quartile value (*Student t-test*, $p < 0.001$) (CC, cancer control; HC, healthy control; LM, leptomeningeal metastasis; BM, brain metastasis; BT, brain tumor. OC, other disease).



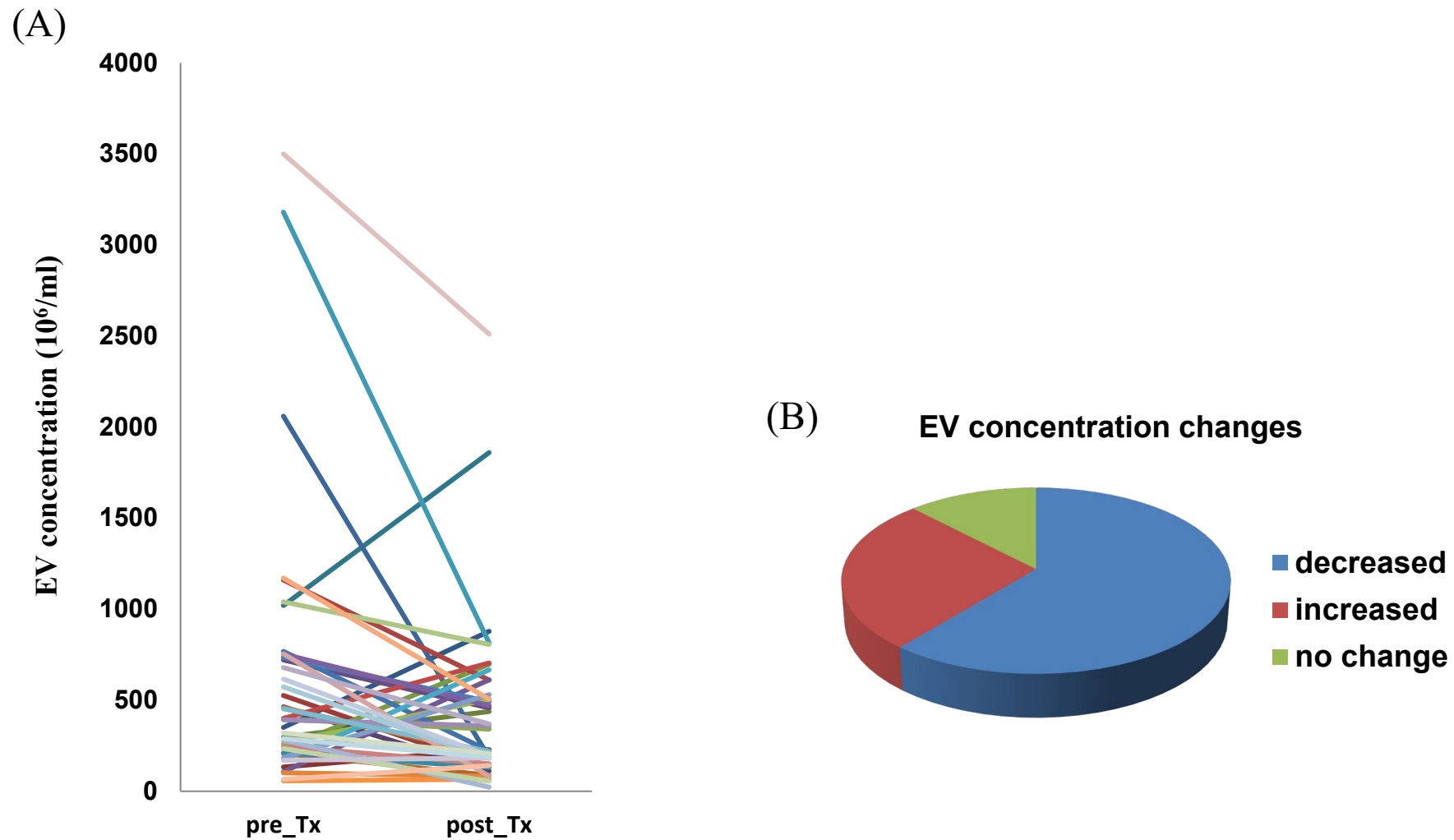
Supplementary figure 3. Evaluation of components of nano-range peaks measured by Dynamic Light Scattering (DLS) using Zetasizer Nano system. (A) Untreated human CSF shows two peaks as described in the text. (B) The small peak was abolished with exosome purification/nucleic acid elimination kit (Exospin®) while the large peak remains.



Supplementary figure 4. Different (A) concentration and (B) size of EV in other CNS disease group according to disease entity of autoimmune disease, intracranial hemorrhage and CNS infection (ANOVA, *Dunn's Multiple Comparison*, * $p < 0.05$)



Supplementary figure 5. Different patterns of NTA-measured particles before (black line) and after (red line) proteinase treatment (A) Shift of larger particles (> 200 nm) with decreased NTA particles, and (B) Shift of larger particles (> 200 nm) with increased NTA particles (C) Relative ratio of NTA particles according to different CNS disease status. The LM group showed significant higher proportion of non-vesicular, proteinase vulnerable particles compared with other groups (*paired t-test*, $*p < 0.05$). PTK, proteinase K; HC, healthy control; LM, leptomeningeal metastasis; BM, brain metastasis.



Supplementary figure 6. Illustration of extracellular vesicle (EV) concentration change after intra-cerebrospinal fluid chemotherapy. (A) Matched pre-treatment and post-treatment exosome concentration of individual patients ($n=41$), (B) Proportion of exosome concentration change of increase, no change ($< \pm 20\%$) and decrease after the treatment.