Expanded View Figures

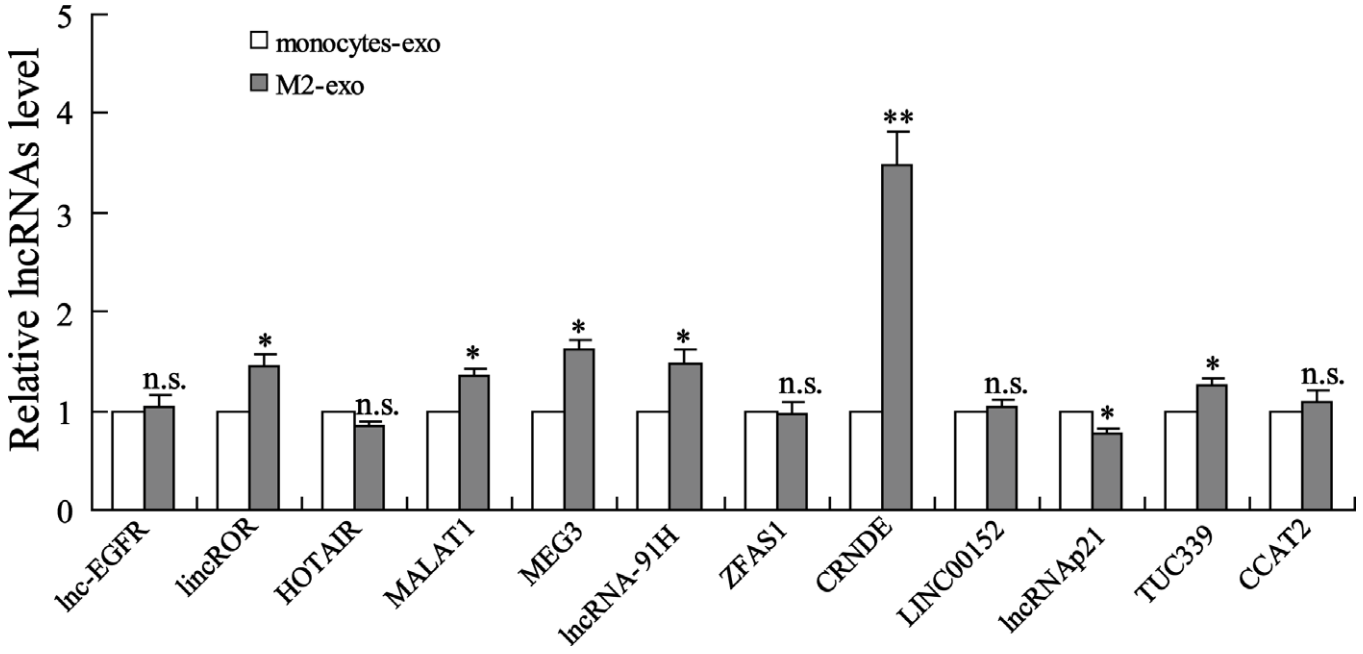

Figure EV1. LncRNA CRNDE is upregulated in M2-polarized macrophage-derived exosomes (M2-exo).

LncRNA expressions in monocytes-derived exosomes (monocytes-exo) and M2-exo were measured by qRT–PCR. The results shown are from three biological replicates and are expressed as mean ± SD. Student's *t*-test. $*P < 0.05$, $**P < 0.01$ vs. monocytes-exo.

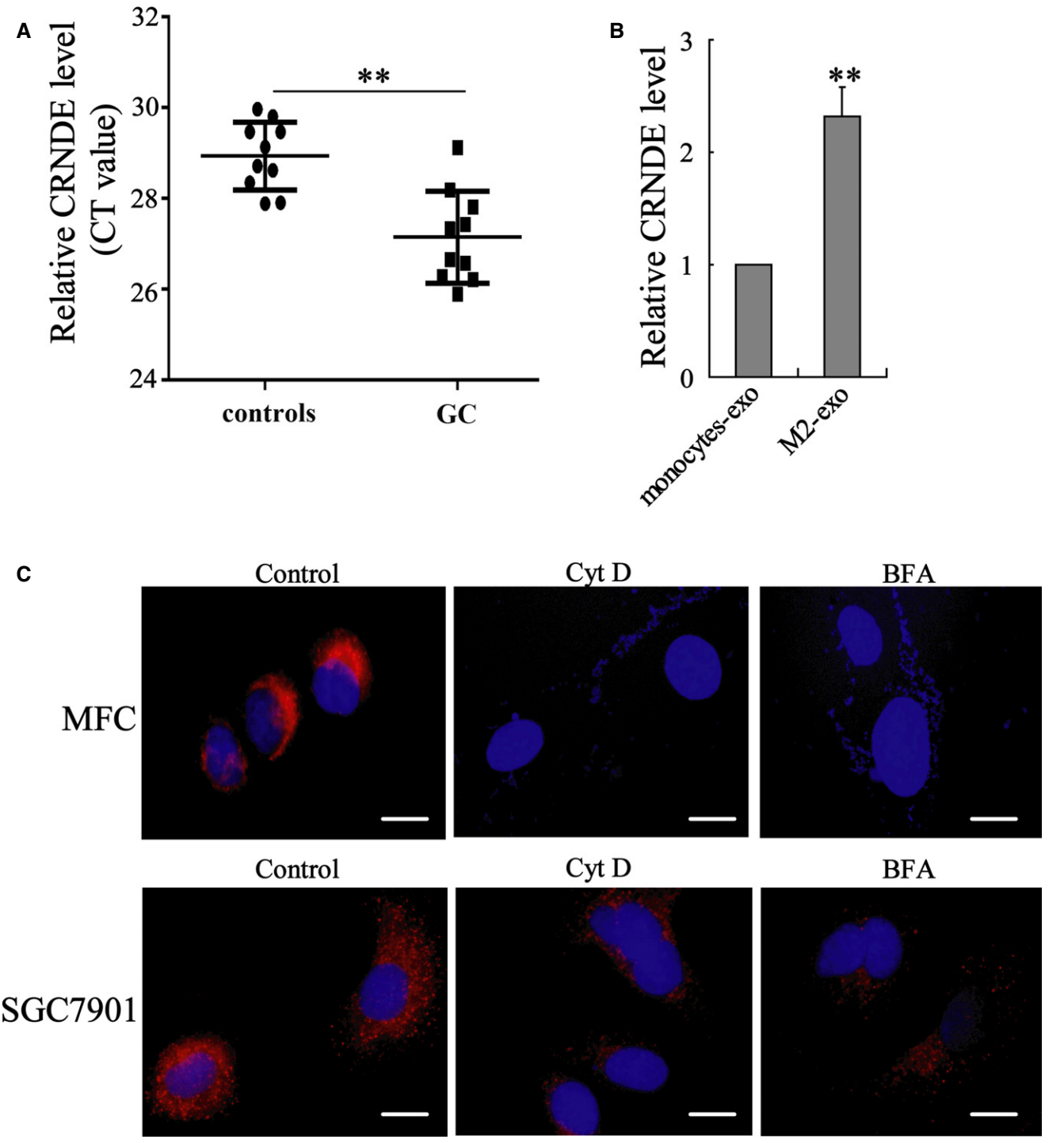

Figure EV2. Overexpressed LncRNA CRNDE in M2-exo-treated GC cells was transferred via exosomes rather than diffusion from the media due to exosomes dissociation.

A Relative LncRNA CRNDE level in GC patients (n = 10) and healthy controls (n = 10) (the serum CRNDE levels were shown as CT values, and higher CT values indicate lower CRNDE levels). Data are expressed as mean ± SD. Student's t-test.

B LncRNA CRNDE expression in MGC-803 cells incubated with monocytes-exo or M2-exo was measured by qRT–PCR. **P < 0.01 vs. monocytes-exo. The results shown are from three biological replicates and are expressed as mean ± SD. Student's t-test.

C MFC and SGC7901 cells were incubated with Cy3-CRNDE-EXO (red) and cytochalasin D (Cyt D; 10 mg/ml) or brefeldin A (BFA; 20 mg/ml). Confocal microscopy was used to detect the Cy3-labeled CRNDE in cells. The nuclei were stained with DAPI (blue). Scale bar = 20 μm.

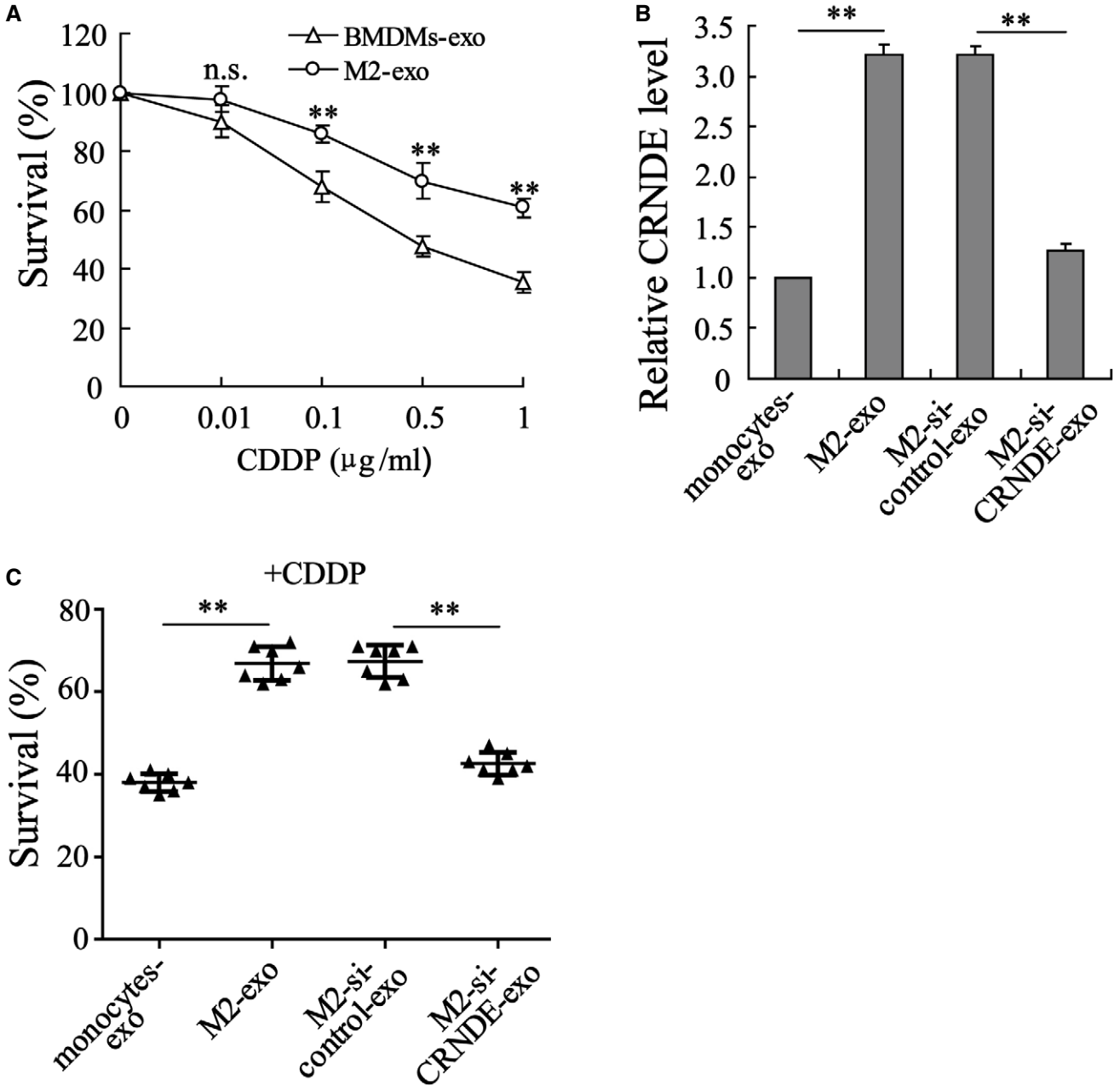

Figure EV3. The exosomal transfer of LncRNA CRNDE induces CDDP resistance in GC cells.

A MFC cells were incubated with CDDP (0, 0.01, 0.1, 0.5, and 1 μg/ml) and BMDMs-exo/M2-exo, and then, the cell survival rate was measured.

B, C Exosomes were isolated from the medium of monocytes (monocytes-exo), monocyte-polarized M2 macrophages (M2-exo), monocyte-polarized M2 macrophages transfected with si-CRNDE (M2-si-CRNDE-exo), and monocyte-polarized M2 macrophages transfected with si-control (M2-si-control-exo). Then, MGC-803 cells were treated with indicated exosomes and CDDP (1 μg/ml) for 48 h. (B) LncRNA CRNDE expression and (C) cell survival rate were measured.

Data information: The results shown are from three biological replicates and are expressed as mean ± SD. (A and B): one-way ANOVA; (C): Student's *t*-test. (A): $^{**}P < 0.01$ vs. BMDMs-exo; (B, C): $^{**}P < 0.01$

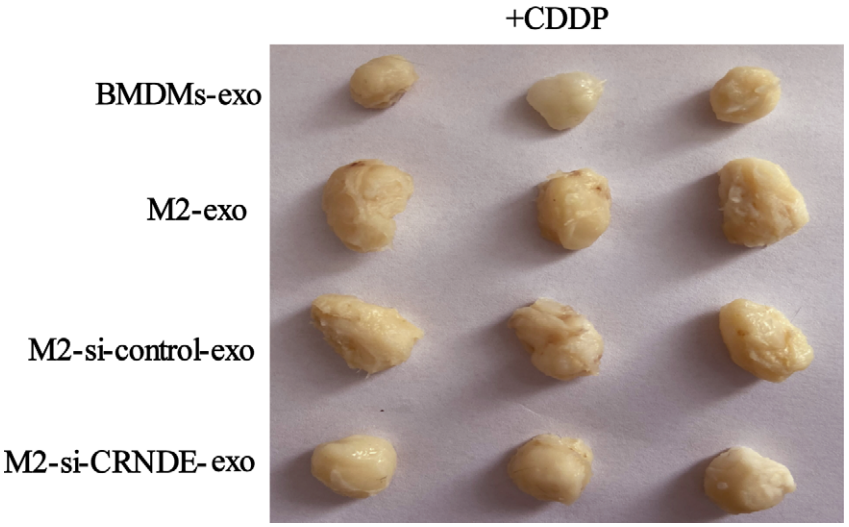

Figure EV4. Patient-derived xenograft model.

The tumor photos of xenografts tumors treated with CDDP + BMDMs-exo, CDDP + M2-exo, CDDP + M2-si-control-exo, or CDDP + M2-si-CRNDE-exo.

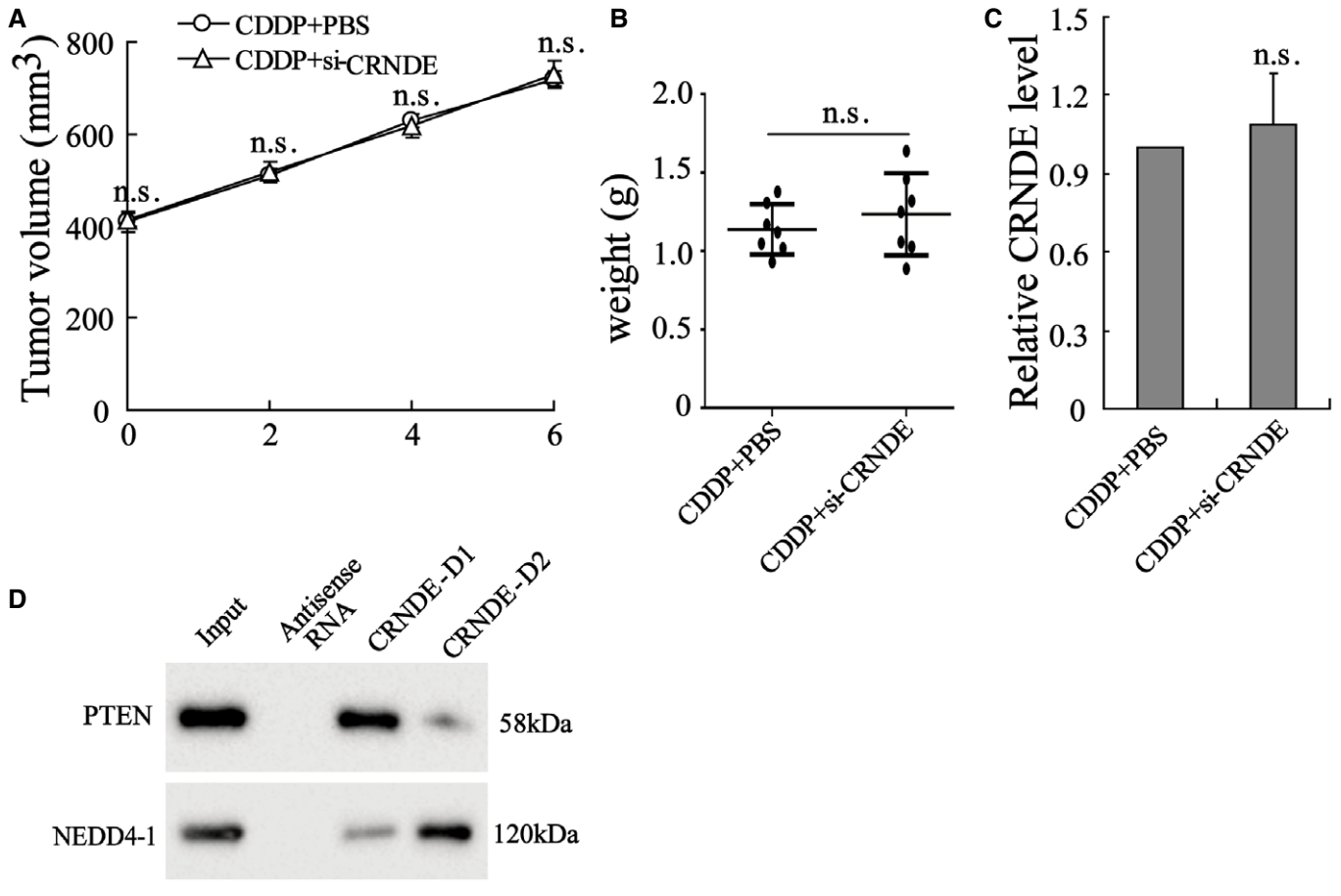

Figure EV5.

Figure EV5. si-CRNDE fails to affect CDDP sensitivity of cancer cells *in vivo* and the interplay between LncRNA CRNDE, PTEN, and NEDD4-1.

Mice were divided into CDDP + PBS and CDDP + si-CRNDE groups. 3×10^5 MFC cells resuspended in 200 μl PBS were subcutaneously injected into nude mice; ten days after injection, si-CRNDE (in PBS media) or its negative control (PBS) was injected into the center of the homograft tumors of mice, followed by a single intraperitoneal injection of CDDP. The (A) tumor volume, (B) tumor weight, and (C) CRNDE expression in the homograft tumors of CDDP-treated mice. (D) Biotinylated CRNDE-D1 (1–500 nt)/CRNDE-D2 (501–1,059 nt) RNAs were incubated with SGC7901 cell lysates, followed by Western blot. The results shown are from three biological replicates and are expressed as mean ± SD.

Source data are available online for this figure.