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Supplementary Materials

Extracellular vesicles from iPSC-MSCs alleviate chemotherapy-induced mouse ovarian damage via the ILK-PI3K/AKT pathway

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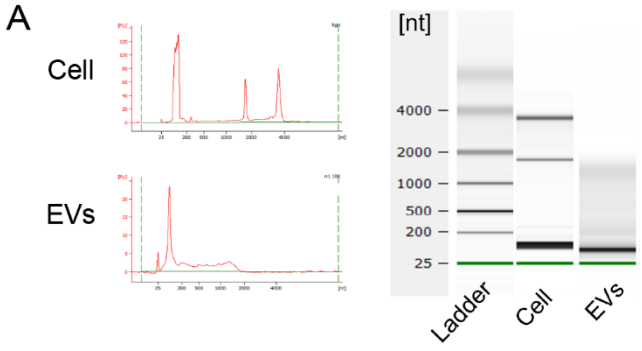
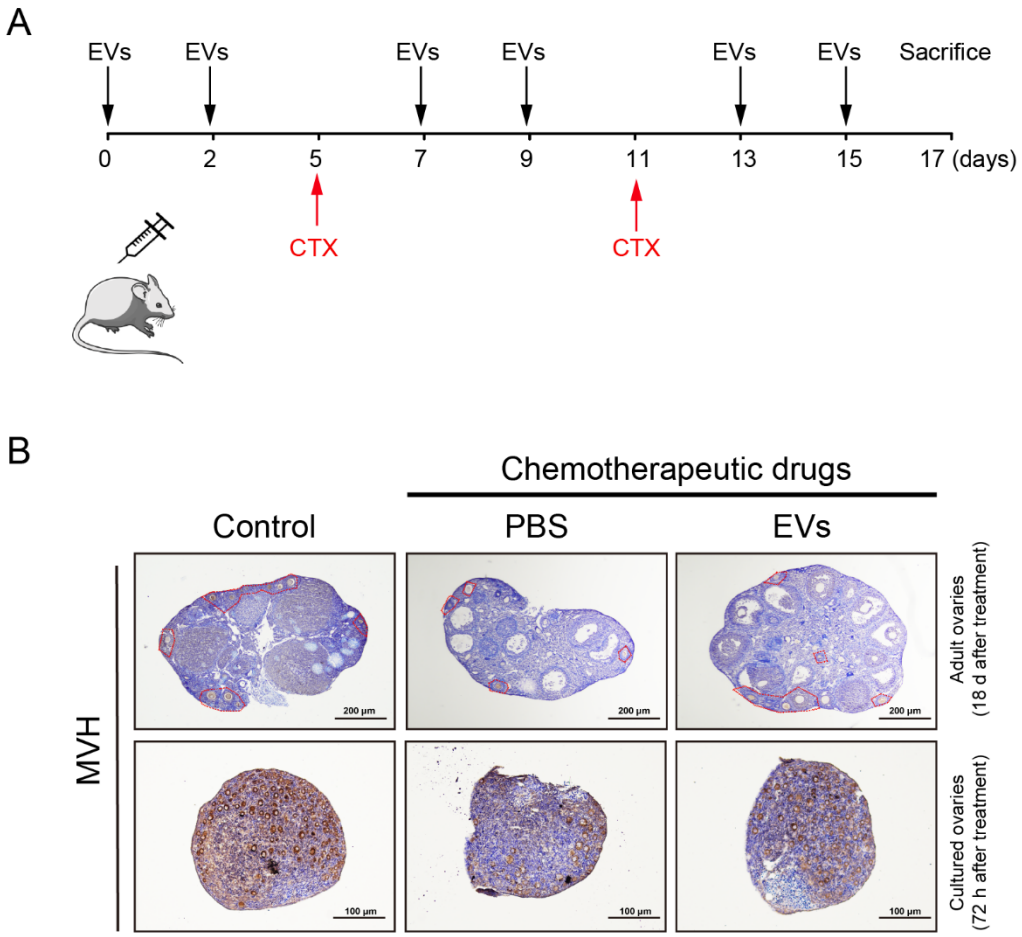
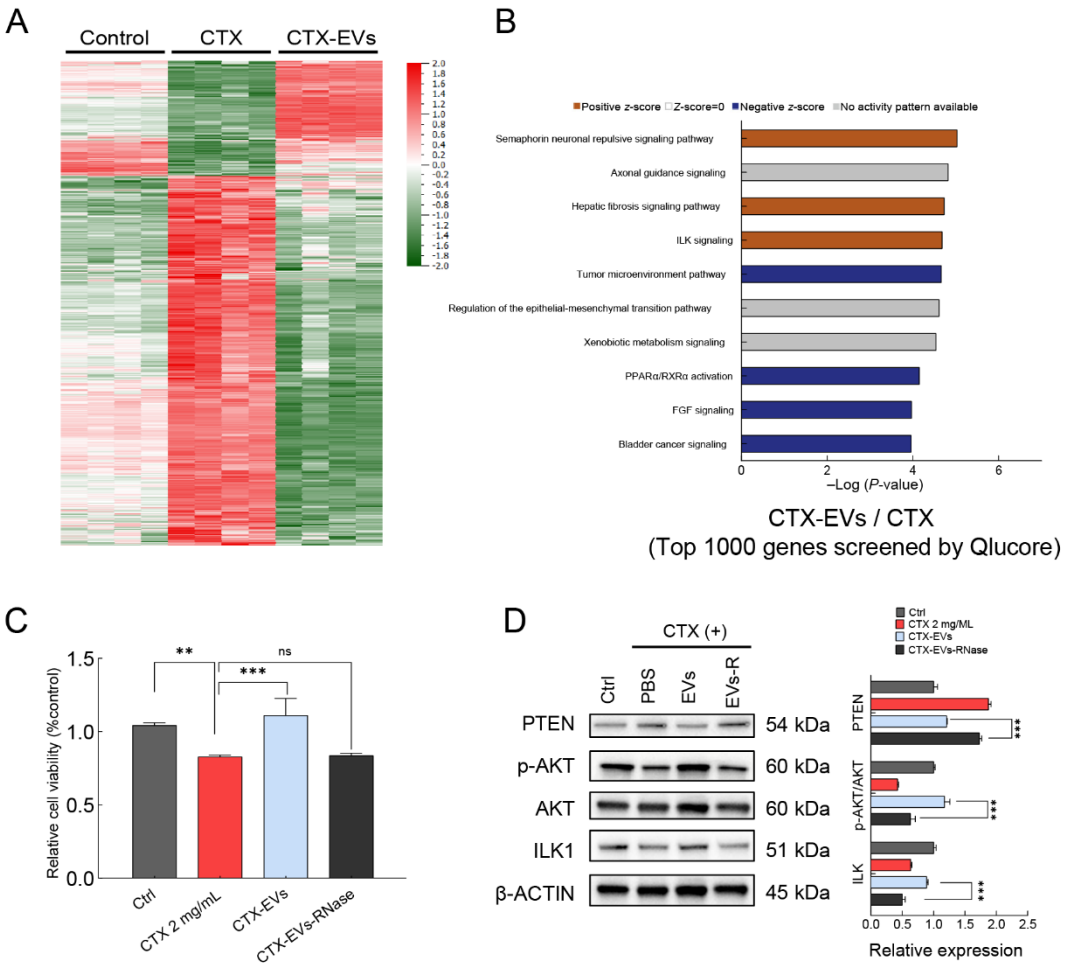


Supplementary Figure S1 Distribution of RNA extracted from iPSC-MSC-EVs (assessed by Agilent 2100 Bioanalyzer)



Supplementary Figure S2 Animal experiment schedule and IHC staining of MVH in mouse ovaries.

A: Experimental schedule of CTX administration and treatment with PBS or iPSC-MSC-EVs in adult mice. B: IHC staining of MVH marker of germ cells in sections of adult and cultured ovaries. Red broken line shows MVH-positive germ cells in adult ovaries. Results indicated that exosomes protected against reduction in germ cell numbers caused by chemotherapy in both adult and *in vitro*-cultured ovaries.



Supplementary Figure S3 The upregulation of the ILK-PI3K/AKT pathway by iPSC-MSC-EVs is abolished after degradation of EV-containing RNA by RNase

A: Heatmap of 1 000 significantly differentially expressed genes (DEGs) screened with Qlucore software. B: Expression ratios of 1 000 DEGs (screened by Qlucore) between CTX-EV and CTX groups analyzed using Ingenuine Pathway Analysis (IPA). Top 10 affected pathways are shown. Yellow column means this pathway is predicted to be activated and blue column means this pathway is predicted to be inhibited. ILK was among the top four significantly changed pathways. C: Granulosa cell viability in control, CTX (2 mg/mL), CTX co-treated with iPSC-MSC-EVs (20 μg/mL), and CTX co-treated with iPSC-MSC-EV-RNase (20 μg/mL) groups, determined by MTS assay (n=3). D: Western blot analysis of expression of ILK, AKT, phosphorylated AKT (Ser 473), and PTEN in control, CTX (2 mg/mL), CTX co-treated with iPSC-MSC-EV (20 μg/ml), and CTX co-treated with iPSC-MSC-EV-RNase (20 μg/mL) granulosa cells. Quantitative protein analysis was performed by ImageJ (right panel).