

Supplementary Materials

Engineered *Panax notoginseng* nanovesicles enhance peptide delivery in intracerebral hemorrhage

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Supplementary Table 1. Primer sequences used for qRT-PCR

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
IL-1 β	GCCTCGTGCTGTCGGACCCATAT	TCCTTTGAGGCCCAAGGCCACA
IL-6	CTTCCATCCAGTTGCCTTCT	CTCCGACTTGTGAAGTGGTATAG
TNF- α	GATCGGTCCCCAAAGGGATG	CCACTTGGTGGTTTGTGAGTG
β -actin	CATTGCTGACAGGATGCAGAAGG	TGCTGGAAGGTGGACAGTGAGG

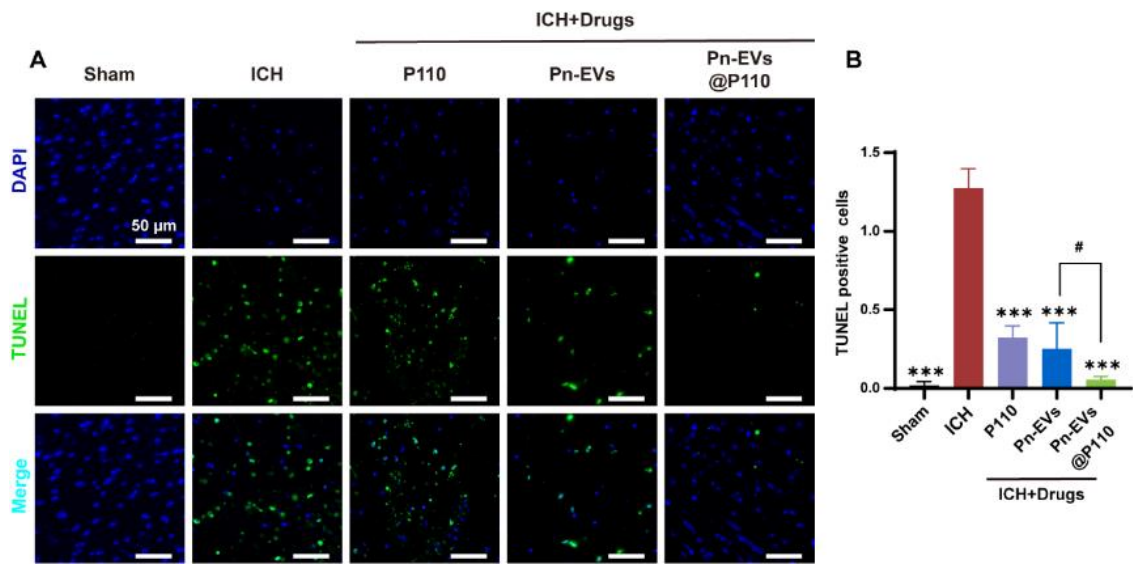
qRT-PCR: Quantitative real-time polymerase chain reaction; IL-1 β : interleukin-1 β ; IL-6: interleukin-6; TNF- α : tumor necrosis factor- α .

Supplementary Table 2. Primary and secondary antibodies used in this study

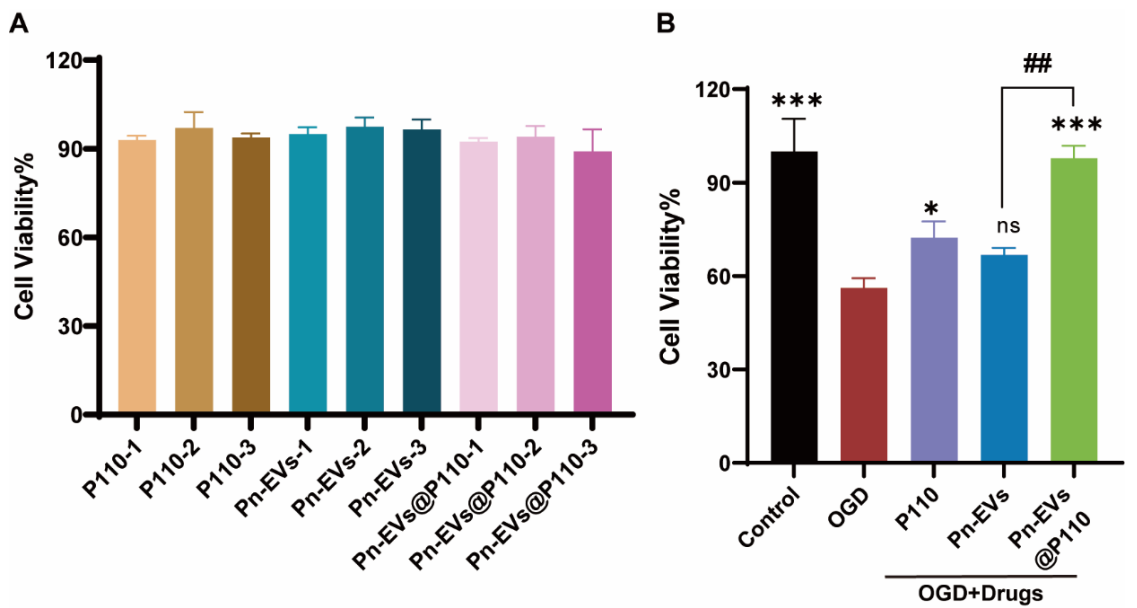
Application	Target	Host species	Catalog No.	Supplier	Dilution
IHC/IF	Iba1	Rabbit	019-19741	FUJIFILM Wako Pure Chemical Corporation	1:1,000
IF	NeuN	Mouse	266 004	Synaptic Systems	1: 500
IF	TOM20	Rabbit	42406	Cell Signaling Technology	1: 500
WB	Phospho-DRP1 (Ser616)	Rabbit	3455	Cell Signaling Technology	1:1,000
WB	DRP1	Rabbit	ab184247	Abcam	1:1,000
WB	MFN2	Rabbit	ab124773	Proteintech	1:1,000
WB	OPA1	Rabbit	ab157457	Abcam	1:1,000
WB	β -actin	Mouse	MA5-15739	Thermofisher	1:1,000
Secondary (WB)	Goat anti-rabbit IgG-HRP	Goat	ab6721	Abcam	1:5,000
Secondary (WB)	Goat anti-mouse IgG-HRP	Goat	31430	Thermofisher	1:5,000
Secondary (IF)	Alexa Fluor 488 goat anti-rabbit IgG	Goat	A27034	Thermofisher	1:5,000
Secondary (IF)	Alexa Fluor 594 goat anti-mouse IgG	Goat	A11032	Thermofisher	1:5,000

IHC: Immunohistochemistry; IF: immunofluorescence; WB: Western blot; DRP1: dynamin-related protein 1; MFN2: mitofusin 2; OPA1: optic atrophy 1; Iba-1: ionized

calcium-binding adapter molecule 1; NeuN: neuronal nuclei; TOM20: translocase of outer mitochondrial membrane 20; IgG: immunoglobulin G; HRP: horseradish peroxidase.

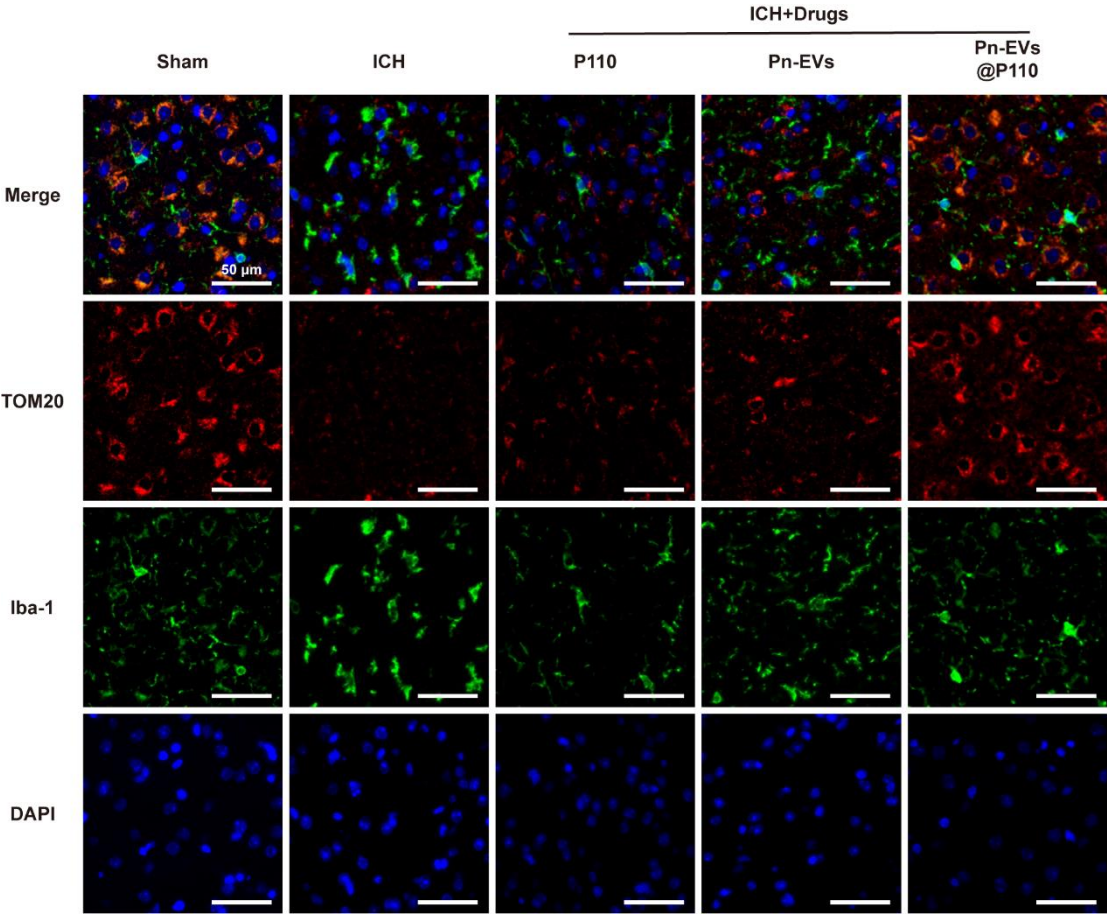


Supplementary Figure 1. (A) Representative TUNEL staining (green) with DAPI counterstain (blue) in perihematomal regions; (B) Quantification of TUNEL-positive cells. Data are presented as mean ± SD. *n* = 3, ****P* < 0.001 vs. ICH; #*P* < 0.05 vs. Pn-EVs. TUNEL: terminal deoxynucleotidyl transferase dUTP nick-end labeling; DAPI: 4',6-diamidino-2-phenylindole; ICH: intracerebral hemorrhage; Pn-EVs: Panax notoginseng-derived extracellular vesicle-like nanovesicles; SD: standard deviation.



Supplementary Figure 2. Cytocompatibility and protection under OGD conditions (in vitro). (A) Cell viability under normal conditions after treatment with P110 (1 μM, 5 μM, 10 μM), Pn-EVs and Pn-EVs@P110 (1 × 10⁷ particles/mL, 1 × 10⁸ particles/mL, 1 × 10⁹ particles/mL); (B) Cell viability under OGD conditions following treatment with P110 (1 μM), Pn-EVs or Pn-EVs@P110 (1 × 10⁷ particles/mL).

Data are presented as mean $\pm$ SD from three independent biological experiments ($n = 3$), with three technical replicates per condition in each experiment. * $P < 0.05$, *** $P < 0.001$ vs. OGD; ## $P < 0.01$ vs. Pn-EVs; ns, not significant. OGD: oxygen-glucose deprivation; Pn-EVs: Panax notoginseng-derived extracellular vesicle-like nanovesicles; SD: standard deviation; ns: not significant.



Supplementary Figure 3. Representative immunofluorescence images of TOM20 (red), Iba-1 (green), and nuclei (DAPI, blue) in perihematomal regions across groups. TOM20: translocase of outer mitochondrial membrane 20; Iba-1: ionized calcium-binding adapter molecule 1; DAPI: 4',6-diamidino-2-phenylindole.