

Supplemental Methods

Fraction of SHED-CM

SHED-CM was separated into five fractions according to molecular weight (MW) using Amicon ultra centrifugal filter devices with 3000, 10000, 50000, 30000, or 100000 MW (Millipore, Billerica, MA).¹

Extraction of Exosome from SHED-CM

SHED-CM was subjected to filtration on 0.22-mm pore-filters (Millipore, Billerica, MA), then the CM was ultra-centrifuged at 200,000 ×g for 110 min. The supernatant was used for SHED-CM without exosomes^{2,3}.

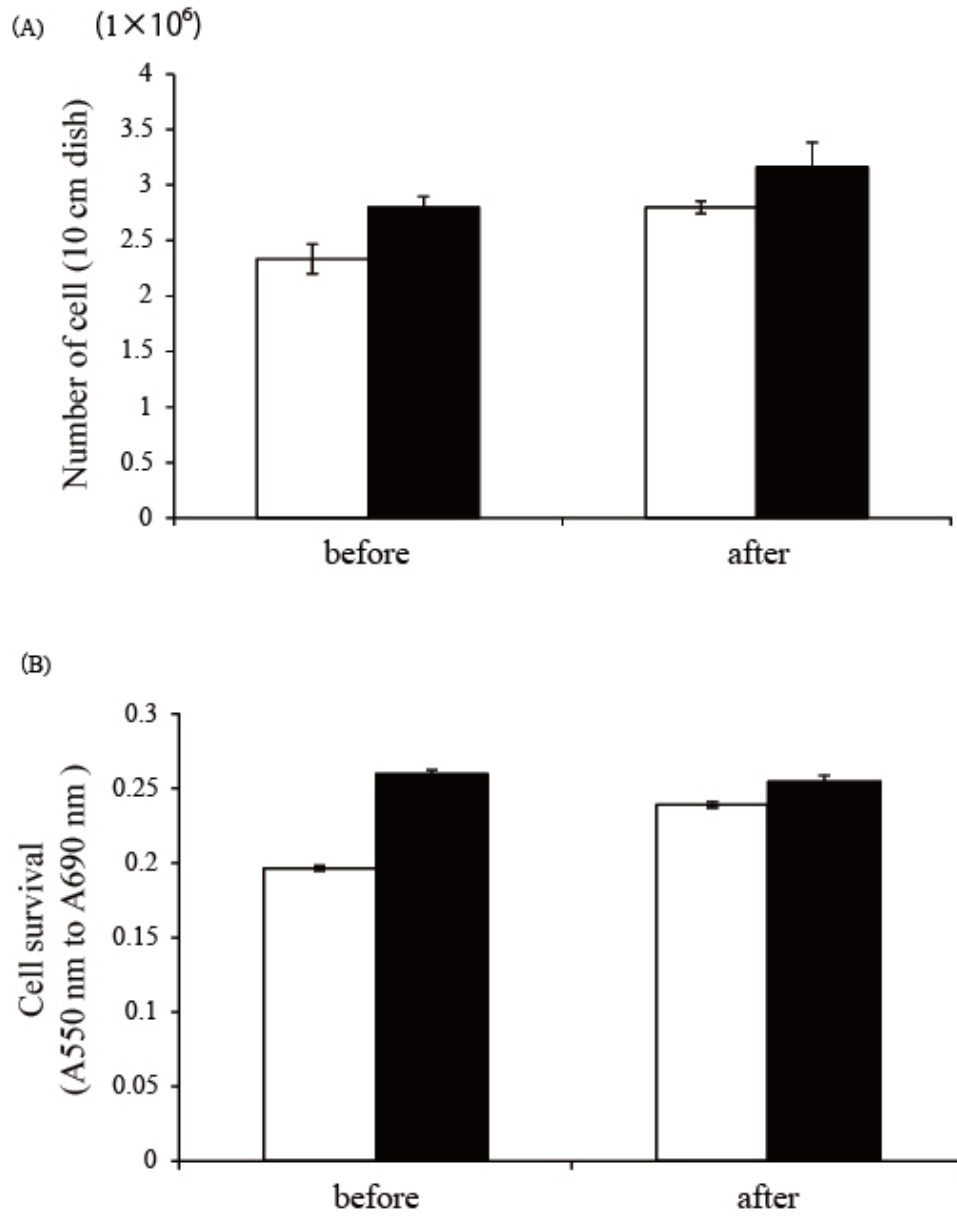
Supplemental Figures:

Supplemental Figure 1 Viability of Stem Cells Cultured in Serum-free Medium

Stem cells were cultured in DMEM with 10% FBS to reach 80% confluence, rinsed three times with PBS, and then cultured in serum-free DMEM for 48 h. The number of cells in a 10-cm dish (A) and MTT assay (B) were examined for the cellular survival before and after incubation in serum-free medium. White bar indicates BM and black

bar indicates SHED. The data is presented as a mean \pm SEM value.

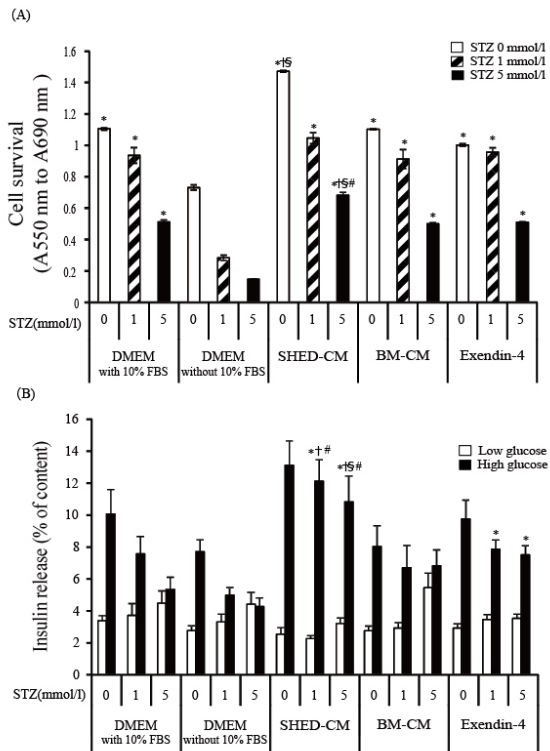
Supplemental Figure. 1



Supplemental Figure 2 Viability and Function of Mouse Pancreatic Cell Line

MIN6 cells were cultured to reach 80% confluence, then incubated with different concentrations of STZ with SHED-CM, DMEM with 10% FBS, DMEM without 10% FBS, Ex-4, or BM-CM for 6 h. Cell survival was examined by MTT assay (A). The MIN6 cells were pre-incubated with a 2.8 mmol/l KRB buffer for 30 min, then stimulated with 2.8 mmol/l (low glucose) or 16.7 mmol/l (high glucose) for 30 min for GSIS (B). The data is presented as a mean \pm SEM value. # P < 0.05 vs DMEM with 10% FBS, * P < 0.05 vs DMEM without 10% FBS; † P < 0.05 vs Ex-4; § P < 0.05 vs BM-CM.

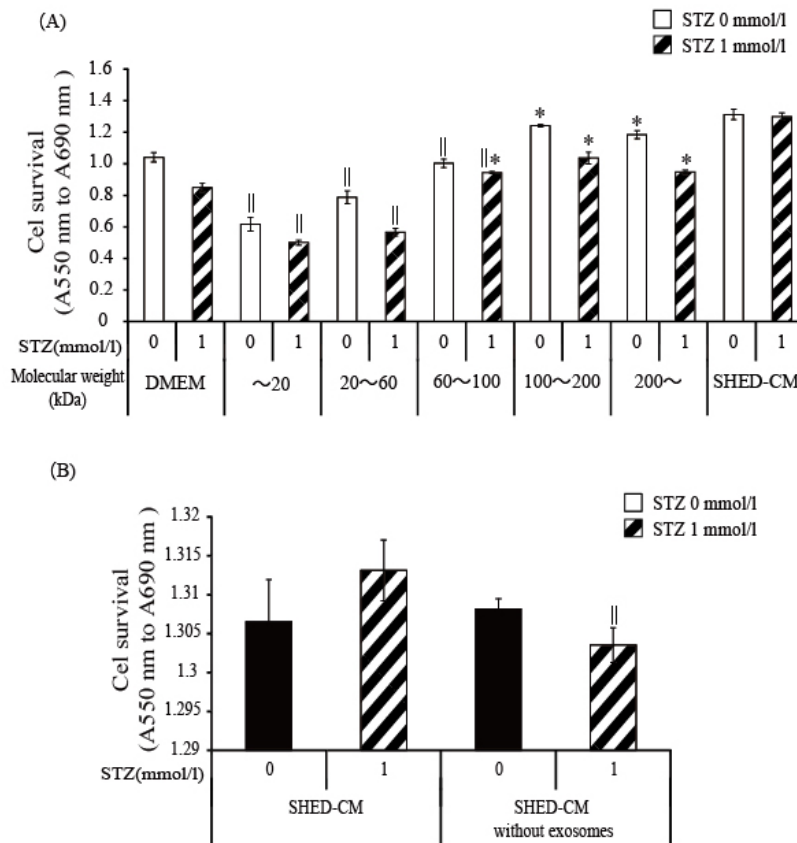
Supplemental Figure. 2



Supplemental Figure 3 Effect of Fraction and Exosomes in SHED-CM on Viability of MIN6 cells

MIN6 cells were cultured to reach 80% confluence, then incubated in different concentrations of STZ with indicated solution for 6 h. The effect of fraction (A) and exosomes (B) in SHED-CM on cell survival were examined by MTT assay. The data is presented as a mean \pm SEM value. * $P < 0.05$ vs DMEM; || $P < 0.05$ vs SHED-CM

Supplemental Figure. 3



References

1. Bai L, Lennon DP, Caplan AI, et al. Hepatocyte growth factor mediates mesenchymal stem cell-induced recovery in multiple sclerosis models. *Nature neuroscience* 2012;**15**(6):862-70.
2. Pivoraite U, Jarmalaviciute A, Tunaitis V, et al. Exosomes from Human Dental Pulp Stem Cells Suppress Carrageenan-Induced Acute Inflammation in Mice. *Inflammation* 2015.
3. Melo SA, Sugimoto H, O'Connell JT, et al. Cancer exosomes perform cell-independent microRNA biogenesis and promote tumorigenesis. *Cancer cell* 2014;**26**(5):707-21.