Supporting information for

Enhancing therapeutic effects and *in vivo* tracking of adipose tissue derived mesenchymal stem cells for liver injury using bioorthogonal click chemistry

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Results

Table S1. The detailed information of peptide sequences

Name	**Sequence**
RK	RLTRKRGLK
DBCO-RK	DBCO-RLTRKRGLK
FITC-RK	FITC-RLTRKRGLK (C-terminal modification)
FITC labeled DBCO-RK	DBCO-RLTRKRGLK-FITC
AK	AAAAAAGLK
DBCO-AK	DBCO-AAAAAAGLK

The letters in red represent mutations.

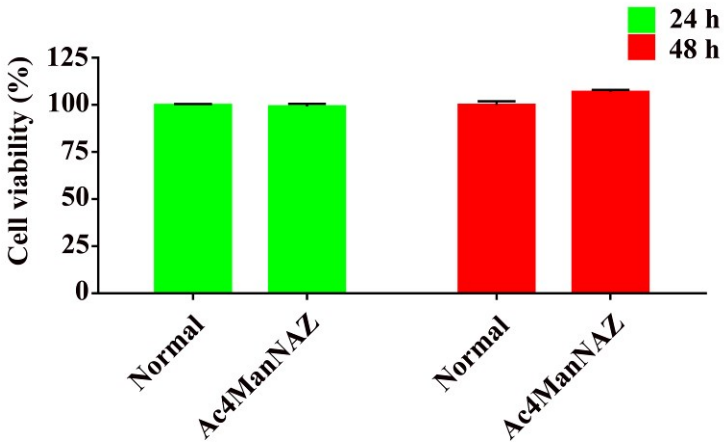

Fig.S1. The relative cell viability of ADSCs after incubation with Ac4ManNAz (50 μM) for 24 h and 48 h, respectively.

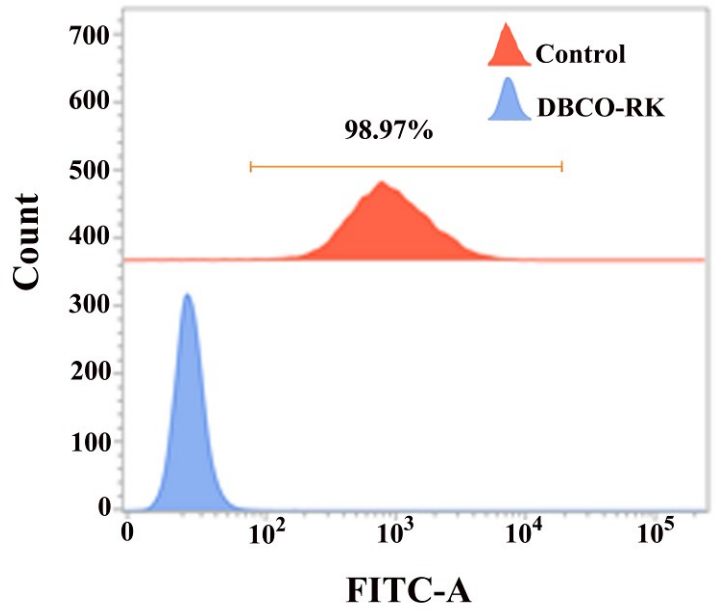

Fig.S2. The modification rate of RK on ADSCs.

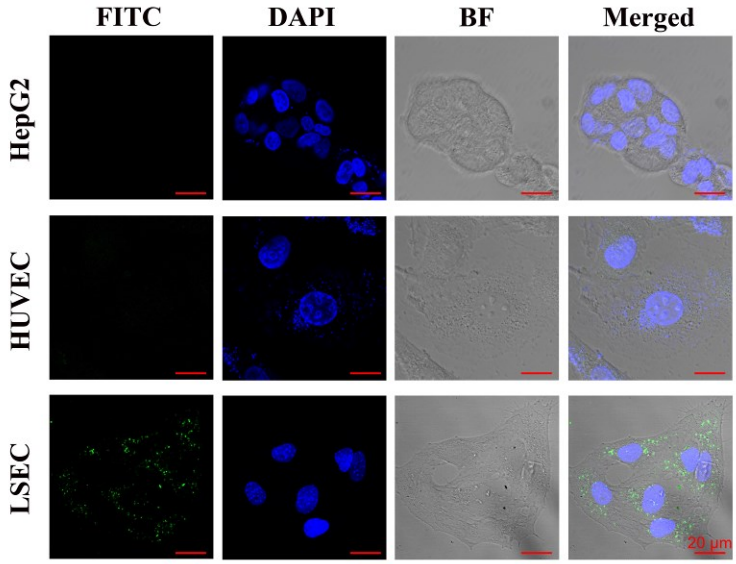

Fig.S3. The specific targeting of RK on LSECs. Scale bar, 20 μm.

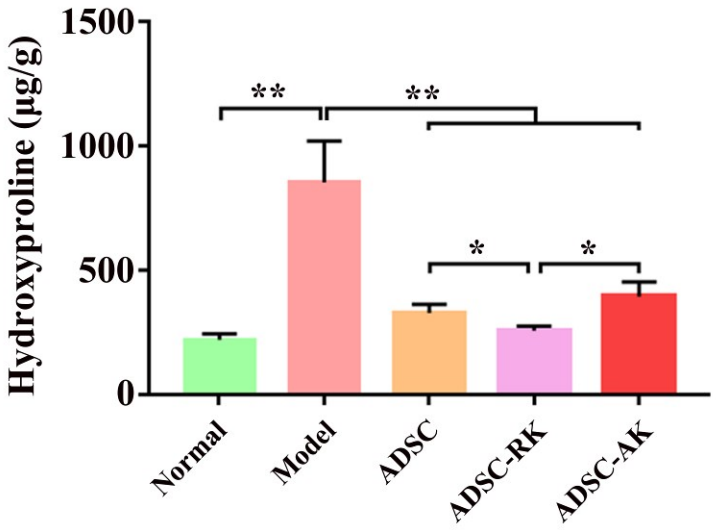

Fig.S4. The hydroxyproline content of liver tissues after ADSC therapy for liver fibrotic mice. (**p<0.01; *p<0.05; n=4 per group).

Experimental

Material

N-azidoacetylmannosamine (Ac4ManNAz) and 4, 6-diamidino-2-phenylindole (DAPI) were obtained from Sigma. CCK8 assay kit and PI/Annexin V apoptosis detection kit were purchased from Dojindo Molecular Technologies (Tokyo, Japan). Dil was obtain from Beyotime Biotechnology (Shanghai, China). Deionized water (ddH_2O with a resistivity of 18.2 MΩ cm was obtained by using a Milli-Q Gradient System (Millipore, Bedford, MA, USA) and used for all experiments. All peptides were chemically synthesized by GenScript (Nanjing, China). All other chemicals, if otherwise not specified, were commercially available and used as received.

Cell Culture

The human liver cancer cell line HepG2 (ATCC, Manassas, VA) was cultured with Dulbecco's Modified Eagle's medium (DMEM) containing 10% fetal bovine serum (FBS). Human umbilical vein endothelial cell (HUVEC) was obtained from National Institutes for Food and Drug Control (Beijing, China) and cultured with RPMI 1640 containing 10% FBS. Liver sinusoidal endothelial cells (LSEC) were isolated from mouse liver tissues and purchased from Servicebio (Wuhan, China), and cultured in LSEC specific medium (Servicebio, Wuhan, China). All cells were incubated in a 37 °C humidified incubator containing 5% CO_2.

Cytotoxicity assay in vitro

The cytotoxicity of Ac4ManNAz was evaluated by CCK8 assay. Briefly, ADSCs were seeded into a 96-well plate at the density of 1×10^4 cells/well and co-incubated

with 50 μM Ac4ManNAz for 24 h, 48 h, respectively. After that, the cells were added with CCK8 solution for another 1h and the absorbance at 450 nm was measured in a Spectra Max M5 microplate reader (Molecular Devices, USA).

CLSM imaging of RK specific targeting to LSEC

Mouse LSEC cells or positive control cells (including HUVEC and HepG2 cells) were seeded into a 35 mm-glass bottom petri dishes at a density of 1×10^5 cells per dish and cultured at a 37 °C humidified incubator containing 5% CO_2 over night. Afterwards, the cells were co-incubated with 50 μM RK for 4 h. After washing with PBS buffer, the cells were fixed with 4% paraformaldehyde (PFA) and stained with DAPI. Finally, the cells were imaged with CLSM (LSM 780, Zeiss, Germany).

Biochemical assays of liver function

The hydroxyproline content in fibrotic liver tissues was analyzed by biochemical analysis using a colorimetric assay kit (Nanjing Jiancheng Bioengineering Institute, Nanjing, China) following manufacture's instructions.