**Supplementary Figure Legends**

**Supplementary Fig 1. Induction of the T2D mouse model.** The T2D mouse model was induced by a combination of an 8-week HFD and a single intraperitoneal injection of low-dose STZ (100 mg/kg). **a** Blood glucose was consecutively detected after STZ injection. One week after STZ injection, IPGTT (**b**) and IPITT (**c**) were performed to confirm the establishment of the T2D mouse model. For IPITT (**c**), the results are presented relative to the initial blood glucose levels. The results are presented as the means ± SD. \**p*<0.05, \*\**p*<0.01.



**Supplementary Fig 2. Identification of UC-MSC characteristics.** UC-MSCs were isolated and identiﬁed from full-term fetal umbilical cords. **a** The morphology of UC**-**MSCs. (B-C): Multilineage differentiation of MSCs: adipocytic differentiation (**b**) was detected by Oil Red O staining; osteoblastic differentiation (**c**) was confirmed by Alizarin Red staining; Scale bar: 50 µm. (**d-f**): Immunological phenotypes of MSCs: cultured UC-MSCs consisted of a homogenous mesenchymal population that stained positive for CD90 in 99.76% of cells (**d**) and CD105 in 99.79% of cells (**e**) but negative for CD45 (**f**), which met the international definition of MSCs.

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**Supplementary Fig 3. Biological characteristics and identification of bone marrow-derived macrophages (BMDMs).** BMDMs were isolated and cultured in RMPI-1640 supplemented with 100 ng/ml M-CSF. **a** The morphology of macrophages. **b** Flow cytometry analyses showed that the positive rate of F4/80 in bone marrow-derived cells was over 95%. (**c, d**): M1 macrophage induction, after stimulation with LPS (100 ng/ml) and IFN-γ (50 ng/ml) for 24 hours, and the morphology of macrophages (**c**). The positive rate of CD11c in BMMCs was over 95% (**d**). Abbreviations: BMDMs, bone marrow-derived macrophages. M-CSF, macrophage colony-stimulating factor.



**Supplementary Fig 4. UC-MSCs combined with decitabine did not influence UC-MSCs homing in T2DM mice.** UC-MSCs were CM-Dil (red) labelled in advance. Successfully induced type 2 diabetic mice were treated with UC-MSCs or UC-MSCs combined with decitabine. One week after the infusion, detection of UC-MSCs in the adipose tissue, liver and lung of T2DM recipients using a confocal laser scanning microscope. Scale bar, 100 μm (A) and 50 μm (B). Values are presented as the means ± SD. ns, no significant difference.



**Supplementary Table 1. Primer sequences of target genes (mice)**

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| --- | --- |
| Genes | Primer sequence (5’-3’) |
| β-actin | For: CCAGTTGGTAACAATGCCATG |
|  | Rev: GGCTGTATTCCCCTCCATCG |
| MCP-1 | For: AGGTCCCTGTCATGCTTCTG |
|  | Rev: GCTGCTGGTGATCCTCTTGT |
| TNF-α | For: CCAGACCCTCACACTCAGATC |
|  | Rev: CACTTGGTGGTTTGCTACGAC |
| IL-1β | For: TGGGCCTCAAAGGAAAGAAT |
|  | Rev: CAGGCTTGTGCTCTGCTTGT |
| IL-6 | For: TAGTCCTTCCTACCCCAATTTCC |
|  | Rev: TTGGTCCTTAGCCACTCCTTC |
| IL-4 | For: GGTCTCAACCCCCAGCTAGT |
|  | Rev: GCCGATGATCTCTCTCAAGTGAT |
| IL-10 | For: GCTCTTACTGACTGGCATGAG |
|  | Rev: CGCAGCTCTAGGAGCATGTG |
| Nos2 | For: ACCTTGGTGAAGGGACTGAG |
|  | Rev: TCCGTTCTCTTGCAGTTGAC |
| CD11c | For: ACGTCAGTACAAGGAGATGTTGGA |
|  | Rev: ATCCTATTGCAGAATGCTTCTTTACC |
| CD206 | For: TGATTACGAGCAGTGGAAGC |
|  | Rev: GTTCACCGTAAGCCCAATTT |
| Arg1 | For: AGACCACAGTCTGGCAGTTG |
|  | Rev: CCACCCAAATGACACATAGG |
| TGF-β | For: ATTCCTGGCGTTACCTTGG  Rev: AGCCCTGTATTCCGTCTCCT |
|  |
| DNMT1 | For: TGAGGAAGGCTACCTGGCTA |
|  | Rev: ACAACCGTTGGCTTTTTGAG |
| DNMT3a | For: TCGGACCCCGCAACTC |
|  | Rev: CAAGCCCTCGGAAAAGTGC |
| DNMT3b | For: GCCAGACCTTGGAAACCTCA |
|  | Rev: GCTGGCACCCTCTTCTTCAT |