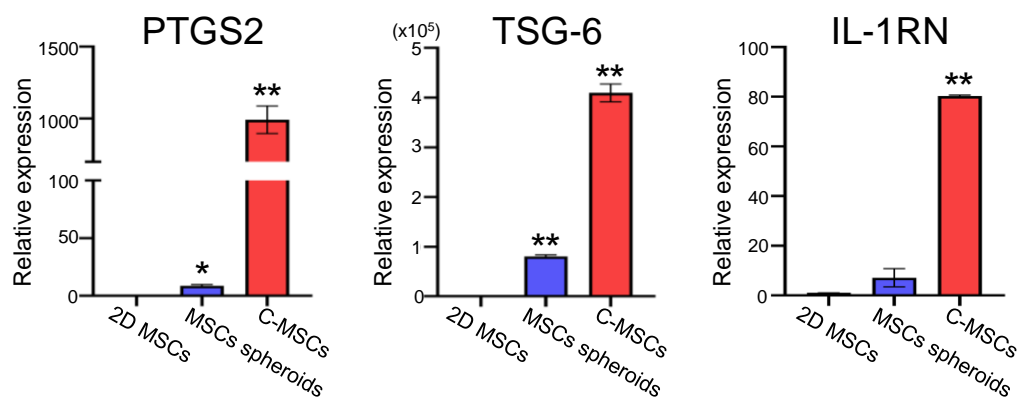


**Supplementary Figure S1. RNA expression patterns quantified using TPM in RNA-seq.**

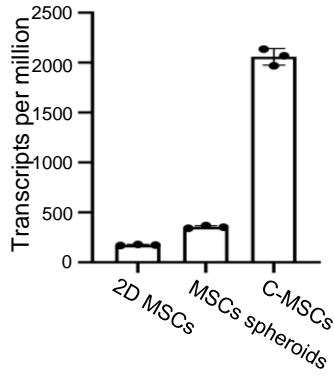
Total RNA was extracted from three distinct cell culture groups: (1) 2D cultures in 24-well plates seeded at  $2.0 \times 10^5$  cells/well ( $n=3$ ), (2) a set of eight MSC spheroids, each consisting of  $2.5 \times 10^4$  cells ( $n=3$ ), and (3) a single C-MSCs formed from  $2.0 \times 10^5$  cells ( $n=3$ ). Then, RNA-seq analysis was performed to assess the expression levels of immunomodulatory factors, cytoprotective factors, and trilineage-related genes. Expression levels of mRNA were quantified as TPM. Values represent means  $\pm$  S.D. of three culture.



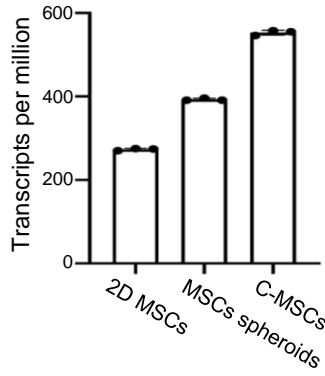
### Supplementary Figure S2. Validation of RNA-seq analysis by qPCR.

Total RNA was extracted from three distinct cell culture groups: (1) 2D cultures in 24-well plates seeded at  $2.0 \times 10^5$  cells/well ( $n=3$ ), (2) a set of eight MSC spheroids, each consisting of  $2.5 \times 10^4$  cells ( $n=3$ ), and (3) a single C-MSCs formed from  $2.0 \times 10^5$  cells ( $n=3$ ). The mRNA expression levels of PTGS2, TSG-6, or IL-1RN were quantified using real-time PCR with  $\Delta\Delta C_t$  method and 18S rRNA as a reference control. Data were normalized to the values of 2D MSCs. Values represent means  $\pm$  S.D. of three cultures. Significant differences compared with 2D MSCs are indicated: \* $p < 0.05$ , \*\* $p < 0.01$  (ANOVA).

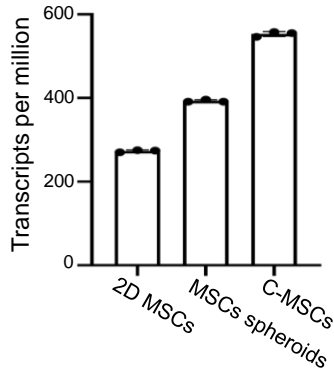
## TWIST



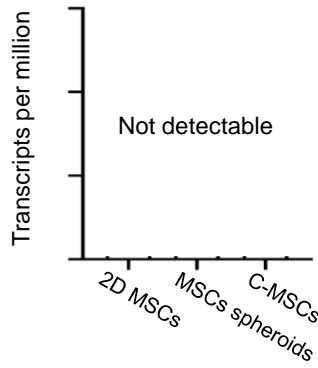
## SNAIL



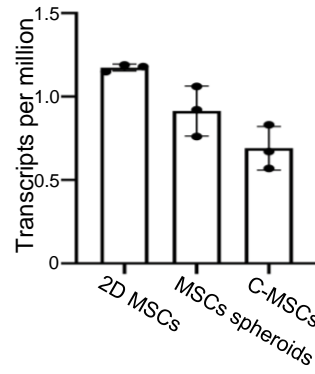
## CD44



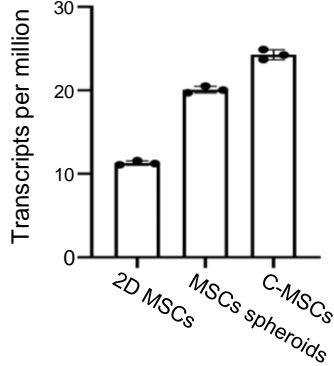
## CD133



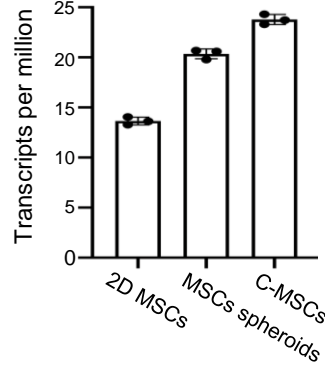
## LAMC2



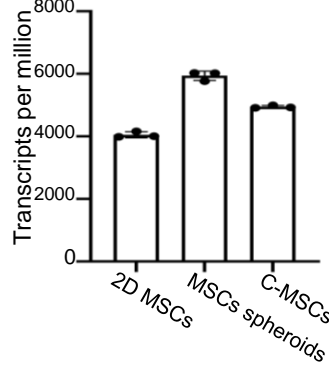
## SMAD2



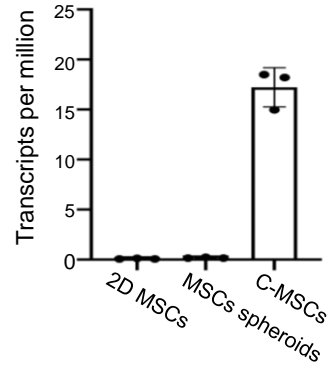
## SMAD4



## MMP2



## MMP10



### Supplementary Figure S3. RNA-seq analysis to assess the expression levels of ECM-related transcription factors, cancer stem cell biomarkers, and TGF- $\beta$ signaling-related genes.

Total RNA was extracted from three distinct cell culture groups: (1) 2D cultures in 24-well plates seeded at  $2.0 \times 10^5$  cells/well ( $n=3$ ), (2) a set of eight MSC spheroids, each consisting of  $2.5 \times 10^4$  cells ( $n=3$ ), and (3) a single C-MSCs formed from  $2.0 \times 10^5$  cells ( $n=3$ ). Then, RNA-seq analysis was performed to assess the expression levels of ECM-related transcription factors, cancer stem cells biomarkers, and TGF- $\beta$  signaling-related genes. Expression levels of mRNA were quantified as TPM. Values represent means  $\pm$  S.D. of three culture.

**Supplementary Table S1. Sense and antisense primers for qPCR**

<i>Target gene</i>		<i>Primer sequence</i>
PTGS2	Forward	5'- TGCATTCTTTGCCCAGCACT -3'
	Reverse	5'- AAAGGCGCAGTTTACGCTGT-3'
IL-1RN	Forward	5'- TTCCTGTTCCATTCAGAGACG-3'
	Reverse	5'- CTTCTGGTTAACATCCCAGATTC-3'
TNFAIP6	Forward	5'- AAGCACGGTCTGGCAAATACAAGC -3'
	Reverse	5'- ATCCATCCAGCAGCACAGACATGA -3'
18S	Forward	5'- GTAACCCGTTGAACCCCAT -3'
	Reverse	5'- CCATCCAATCGGTAGTAGCG -3'