

Supplementary information

Secreted MMP-14 is a predictor for antifibrotic effect of IC-2-engineered mesenchymal
stem cell sheets on liver fibrosis in mice

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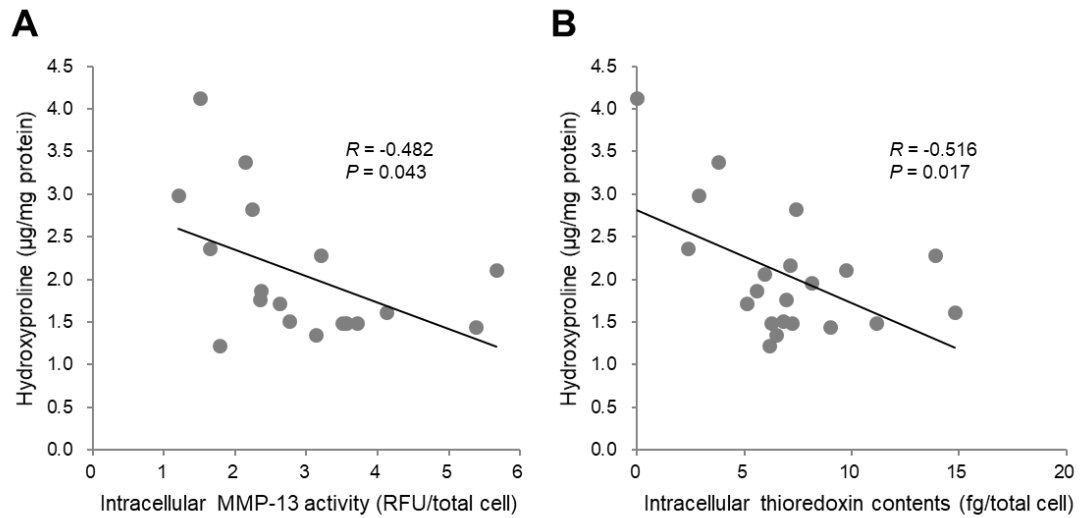


Figure S1. Relationship of hepatic hydroxyproline contents with intracellular MMP-13 activity and thioredoxin contents of IC-2 sheets. **A** Inverse correlation was observed between intracellular MMP-13 activity in pretransplant IC-2 sheets and with hepatic hydroxyproline at 7 days after transplantation. **B** Inverse correlation was observed between intracellular thioredoxin contents in pretransplant IC-2 sheets with hepatic hydroxyproline at 7 days after transplantation.

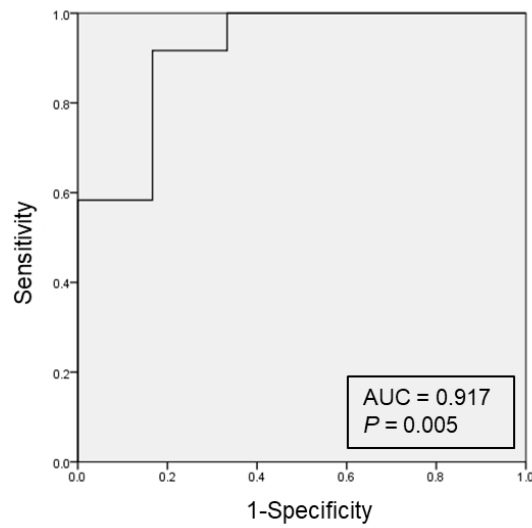


Figure S2. Receiver operating curve (ROC) of secreted MMP-14 contents for therapeutic effects of the IC-2 sheets. ROC curve shows the sensitivity and specificity of secreted MMP-14 contents in predicting inhibitory effect on liver fibrosis of CCl₄-induced chronic liver injury mice. Moreover, >30% suppression of hydroxyproline contents compared with the sham group is regarded as effective.

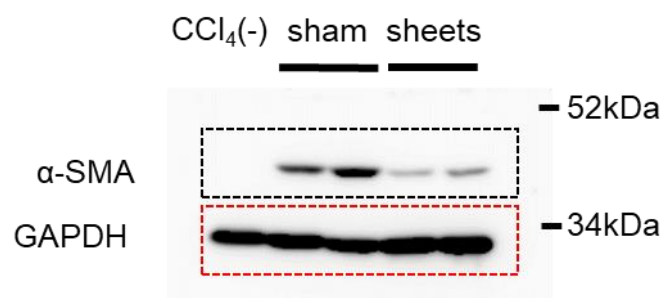


Figure S3. Full-length blots of Fig. 2D. *Black dotted line (α -SMA) and red dotted line (GAPDH) show each cropping location. α -SMA and GAPDH were detected in the same blot. Brightness and contrast were not changed during the processing of these blots.*

Table S1. Information of cell, age, sex, and several parameters in the supernatant of IC-2 sheets.

Lot# (Cell)	Age (year)	Sex	MMP-1 (fg/cell)	MMP-14 (fg/cell)	MMP-2 activity (fg/cell)	MMP-13 activity (fg/cell)	Thioredoxin (fg/cell)	Amphiregulin (fg/cell)	C3 (pg/cell)	Hydroxyproline (μg/mg protein)
2P4	23	F	14.5	0.55	10.3	1.81	0.542	0.071	0.047	4.13
3P4	24	F	26.2	1.52	19.5	3.31	0.221	0.098	0.124	1.48
4P4	23	F	18.8	1.14	20.9	4.13	0.012	0.234	0.135	2.28
6P3	24	F	15.6	0.91	16.9	4.78	0.203	0.208	0.022	2.82
6P4	24	F	28.2	< LOD	19.2	3.64	0.344	0.214	0.033	1.96
7P3	23	F	25.8	0.69	13.8	2.54	0.388	0.089	0.082	2.17
12P3	21	M	11.1	< LOD	34.2	8.57	0.035	0.162	0.033	2.11
15P3	20	M	12.8	0.99	30.9	4.90	0.051	0.168	0.113	1.49
15P4	20	M	24.6	1.49	26.0	4.32	0.530	0.244	0.194	1.49
21P3	33	F	7.0	1.24	15.0	3.81	0.035	0.087	0.018	1.87
21P4	33	F	17.5	0.92	18.9	3.46	0.283	0.111	0.032	1.51
22P3	24	M	5.7	1.80	23.7	3.85	0.165	0.115	0.026	1.76
22P4	24	M	8.8	1.18	16.1	3.24	0.109	0.101	0.024	1.22
23P2	33	M	17.4	0.73	11.5	2.24	0.607	0.059	0.010	2.36
23P4	33	M	4.5	0.58	8.9	2.06	0.214	0.092	0.027	2.99
25P3	26	F	19.0	2.00	24.6	11.43	1.045	0.077	0.055	1.62
27P3	27	M	16.2	1.10	27.9	5.56	0.815	0.133	0.024	1.45
27P4	27	M	9.9	0.99	11.1	2.09	0.497	0.058	0.008	2.07
29P3	33	M	18.5	< LOD	13.8	4.09	0.129	0.056	0.035	3.38
29P4	33	M	29.4	1.19	21.1	5.32	0.167	0.081	0.066	1.35
30P4	29	M	38.6	0.79	83.5	5.32	0.089	0.212	0.028	1.72
Mean ± S.D.			17.6 ± 8.8	1.1 ± 0.4	22.3 ± 15.6	4.3 ± 2.2	0.31 ± 0.28	0.13 ± 0.06	0.05 ± 0.05	2.06 ± 0.7

MMP, matrix metalloproteinase; LOD, limit of detection.

Table S2. Information of cell, age, sex, and several parameters in cell lysates of IC-2 Sheets.

Lot# (Cell)	Age (year)	Sex	Active MMP-1 activity (RFU/cell)	Total MMP-1 activity (RFU/cell)	Active MMP-14 activity (RFU/cell)	Total MMP-14 activity (RFU/cell)	MMP-2 activity (fg/cell)	MMP-13 activity (fg/cell)	Thioredoxin (fg/cell)	Hydroxyproline (μg/mg protein)
2P4	23	F	0.1690	0.1119	0.3392	0.1533	7.264	1.501	0.008	4.13
3P4	24	F	0.2707	0.3585	0.5656	0.2762	16.770	3.560	11.161	1.48
4P4	23	F	0.1844	0.2010	0.3493	0.1666	12.255	3.196	13.904	2.28
6P3	24	F	0.1084	0.1372	0.4096	0.1917	8.536	2.236	7.378	2.82
6P4	24	F	0.2718	0.3247	0.5130	0.2718	6.391	ND	8.107	1.96
7P3	23	F	0.2371	0.3712	0.5735	0.3294	9.462	ND	7.134	2.17
12P3	21	M	0.2946	0.3767	0.6613	0.3198	18.121	5.668	9.747	2.11
15P3	20	M	0.3670	0.3152	0.3923	0.2677	12.768	3.708	6.245	1.49
15P4	20	M	0.3651	0.4363	0.7380	0.4179	12.772	3.505	7.200	1.49
21P3	33	F	0.0396	0.0845	0.3662	0.1204	6.821	2.357	5.548	1.87
21P4	33	F	0.0881	0.0719	0.2831	0.1268	5.430	2.755	6.795	1.51
22P3	24	M	0.1741	0.0679	0.2088	0.1560	5.136	2.350	6.934	1.76
22P4	24	M	0.1828	0.1618	0.2131	0.1137	2.082	1.776	6.146	1.22
23P2	33	M	0.0702	0.0495	0.1119	0.0793	4.970	1.636	2.381	2.36
23P4	33	M	0.0477	0.0442	0.1520	0.1428	4.357	1.196	2.860	2.99
25P3	26	F	0.2232	0.2449	0.7217	0.5434	13.954	4.126	14.804	1.62
27P3	27	M	0.0782	0.1311	0.6762	0.4812	23.589	5.383	8.983	1.45
27P4	27	M	0.0588	0.1152	0.2353	0.3059	3.764	ND	5.942	2.07
29P3	33	M	0.1923	0.1017	0.2062	0.3236	5.381	2.142	3.770	3.38
29P4	33	M	0.1410	0.1281	0.5238	0.3252	7.841	3.132	6.500	1.35
30P4	29	M	0.2376	0.2433	0.4150	0.2208	5.959	2.623	5.109	1.72
Mean ± S.D.			0.18 ± 0.1	0.19 ± 0.1	0.41 ± 0.2	0.25 ± 0.1	9.22 ± 5.5	2.94 ± 1.2	6.98 ± 3.5	2.06 ± 0.7

MMP, matrix metalloproteinase; ND, not detected.

Table S3. Information of age, sex, primary disease, coexisting illness and medication of the elderly patients who underwent artificial joint replacement.

MSC donor	Age	Sex	Primary disease	Coexisting illness	Medication
#1	74	F	coxarthrosis	-	-
#2	67	F	coxarthrosis	-	-
#3	79	M	coxarthrosis	-	-
#4	55	F	coxarthrosis	-	-
#5	59	F	coxarthrosis	-	-
#6	67	F	idiopathic osteonecrosis of femoral head	breast cancer	-
#7	50	M	idiopathic osteonecrosis of femoral head	hepatitis B, portal vein thrombosis, cerebral infarction	warfarin
#8	74	F	coxarthrosis	hypertension, postpneumonectomy pulmonary tuberculosis	-