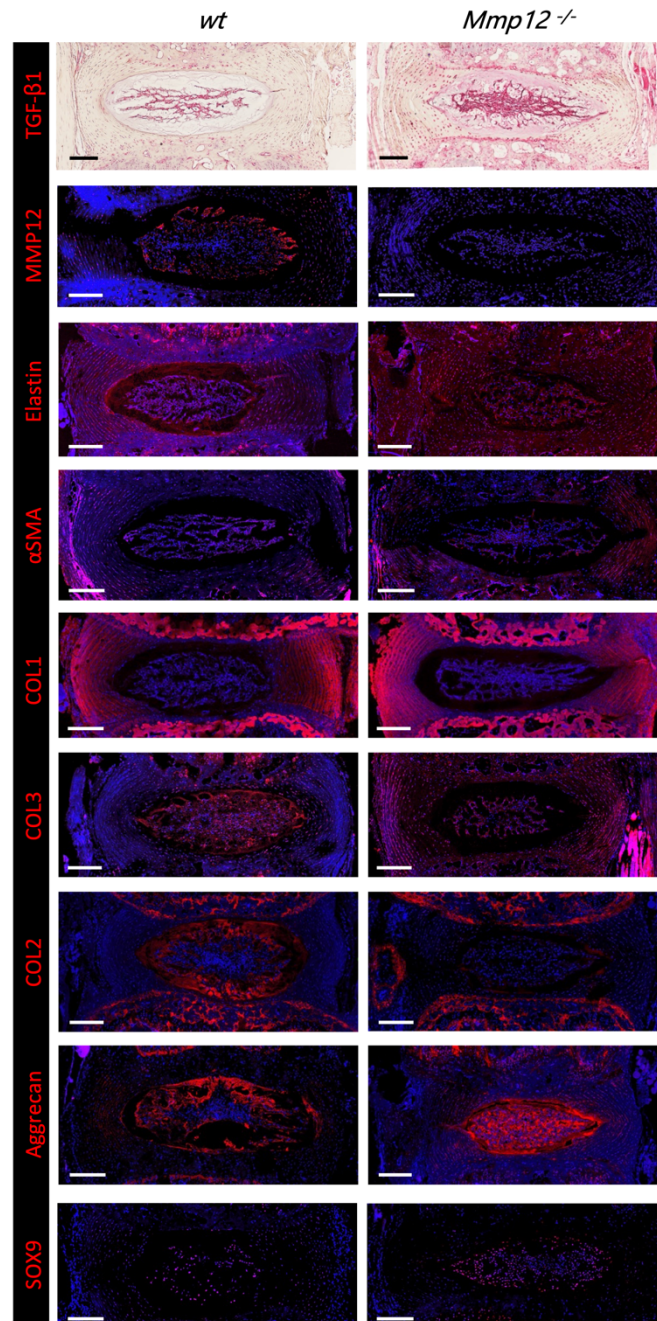
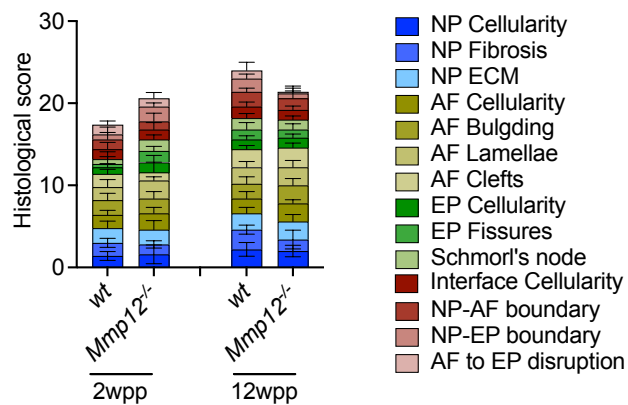


- 1 **Supplementary Figures**
- 2 **Supplementary Figure S1. Immunostaining of TGF- β 1, MMP12, elastin, α SMA,**
- 3 **Sox9, collagen I (COL1), II (COL2) and III (COL3), and aggrecan in un-**
- 4 **operated discs of wild type (*w.t*) and *Mmp12* knockout (*Mmp12*^{-/-}) mice.**
- 5 Representative images are shown. Scale bar: 200um.

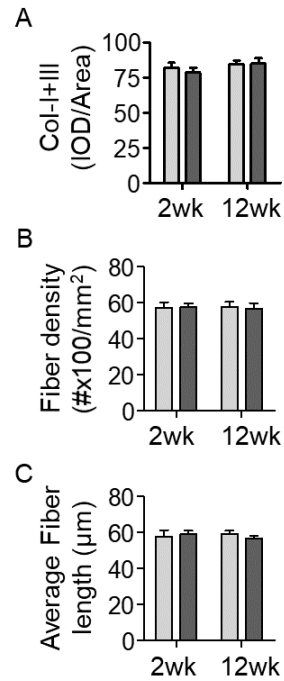


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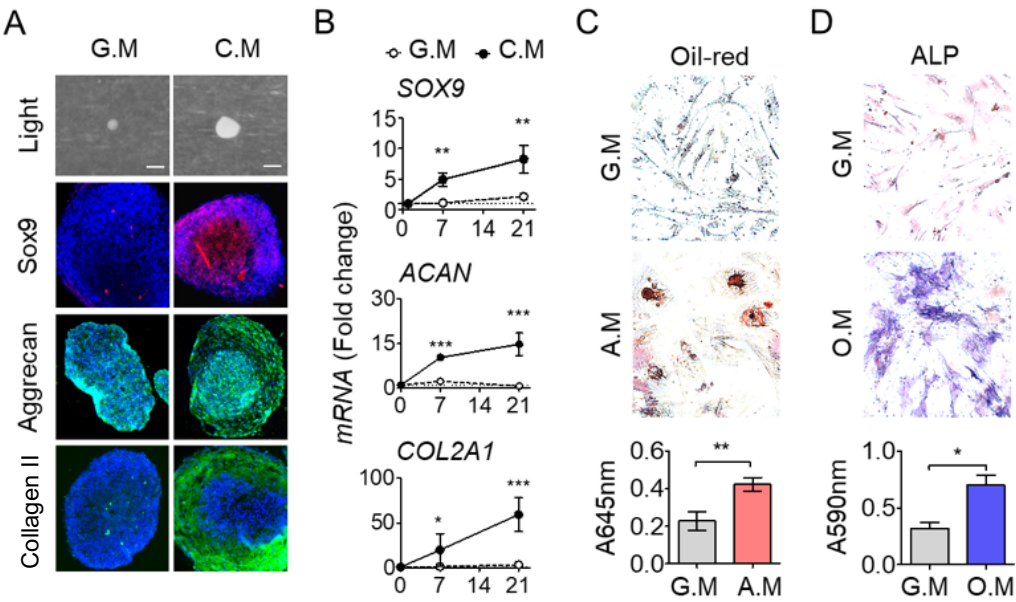
10 **Supplementary Figure S2.** Histological scoring details.



Supplementary Figure S3. Quantification of collagen fiber metrics in annulus fibrosus. (A) Abundance; (B) Density; (C) Length of collagen fibers in AF from punctured disc were calculated by CT-FIRE based on Sirius red stained sections. IOD, integral optical density.



Supplementary Figure S4. Tri-lineage differentiation of MSC. Bone marrow derived mesenchymal stromal cells (MSC) were cultured in basal growth medium (G.M) or medium for chondrogenic (C.M), adipogenic (A.M) or osteogenic (O.M) differentiation (n=3). Chondrogenic differentiation was assessed by protein (A) and gene (B) expression of Sox9, aggrecan and collagen II. (C) Adipogenic differentiation was assessed by oil-red staining. (D) Osteogenic differentiation was assessed by alkaline-phosphatase (ALP) staining. * p<0.05; ** p<0.01; *** p<0.001 determined by two-way ANOVA with Bonferroni post-hoc test for gene expression or unpaired t test for oil-red and ALP quantification.



79 **Supplementary Table 1. Summary of DEGs fold changes of biomarkers for NPC**
80 **subtypes.** Biomarkers were defined based on previous single-cell RNA transcriptome
81 data. DEGs fold changes were extracted from dNPC transcriptome.

NPC subtype	Signature genes	TGF- β 1 treatment		TGF- β 1 + siMMP12 transfection	
		Log10 Fold changes	<i>p</i> value	Log10 Fold changes	<i>p</i> value
ProgNP	<i>SERPINF1</i>	-0.35353	0.02179	-0.06939	0.60959
	<i>FBLN1</i>	-0.76456	0.00000	0.25278	0.00371
	<i>SERPING1</i>	-0.81262	0.00000	-0.00544	0.94846
	<i>PLA2G2A</i>	-1.15865	0.04598	-0.38472	0.51976
	<i>GPX3</i>	-0.81740	0.00000	0.13232	0.03339
	<i>IGFBP6</i>	-0.68152	0.00000	-0.02606	0.78845
	<i>LTBP4</i>	0.06662	0.69464	0.20667	0.01639
	<i>APOD</i>	-0.79058	0.00000	0.11812	0.44944
	<i>TNXB</i>	-1.66075	0.00000	0.55348	0.52363
	<i>PDGFRA</i>	-1.01243	0.00000	0.23163	0.00499
ChonNP	<i>COL2A1</i>	0.05356	0.84048	0.03651	0.79089
	<i>SNORC</i>	-0.29062	0.22196	0.17504	0.49382
	<i>cnmd</i>	-0.38077	NA	-0.28583	0.73431
	<i>caps</i>	-0.42344	0.01422	0.18426	0.29290
	<i>COL9A3</i>	-0.78564	0.00245	-0.15518	0.37372
	<i>SERPINA5</i>	-0.20289	0.39099	0.55912	0.00000
	<i>ACAN</i>	-0.87870	0.00000	0.24575	0.01275
	<i>COL9A3</i>	-0.78564	0.00245	-0.15518	0.37372
	<i>SERPINA3</i>	-0.24034	0.02648	0.10494	0.12232
	<i>CHRD2</i>	-0.75105	0.00346	0.31223	0.15477
FibroNP	<i>COL1A1</i>	0.47739	0.00005	-0.20794	0.00500
	<i>COL3A1</i>	0.68955	0.00003	-0.59605	0.05452
	<i>fn1</i>	0.75311	0.00000	-0.26726	0.00023
	<i>POSTN</i>	0.91195	0.00000	-0.17097	0.05013
	<i>SPARC</i>	0.56591	0.00000	-0.21334	0.00182
	<i>MMP2</i>	0.63070	0.00000	-0.08730	0.57110
	<i>TNC</i>	-0.19623	0.13486	-0.37129	0.00000
	<i>SERPINH1</i>	0.40708	0.00000	-0.19458	0.00111
	<i>COL1A2</i>	0.18973	0.10765	-0.16625	0.03501
	<i>PRSS23</i>	0.17911	0.02630	-0.11760	0.00741
CyclingNP	<i>STMN1</i>	-0.03450	0.90479	-0.55010	0.01575
	<i>PTTG1</i>	0.12637	0.70262	-0.29985	0.09727
	<i>TOP2A</i>	0.16719	0.73264	-0.97406	0.03677
	<i>CENPF</i>	0.18771	0.69962	-0.45732	0.27032
	<i>NUSAP1</i>	0.14769	0.77907	-0.48655	0.17594
	<i>LGALS1</i>	0.32682	0.00001	-0.14202	0.04842
	<i>TUBB</i>	0.41352	0.18634	-0.05530	0.84679

	<i>BIRC5</i>	0.13316	0.80275	-0.51180	0.23991
	<i>TYMS</i>	-0.07246	0.76884	0.09672	0.49409
	<i>SMC4</i>	-0.13361	0.19491	-0.24311	0.00034
RegNP	<i>MMP3</i>	-0.18043	0.45491	0.15506	0.22159
	<i>CHI3L1</i>	-1.29153	0.00000	0.03514	0.86673
	<i>GPX3</i>	-0.81740	0.00000	0.13232	0.03339
	<i>BMP2</i>	-0.33695	0.28731	-0.01535	0.91952
	<i>SOD2</i>	-1.03172	0.00000	-0.15638	0.03082
	<i>C11orf96</i>	0.18211	0.05736	-0.30105	0.00277
	<i>SLC7A2</i>	-0.88895	0.00000	0.18498	0.12220
	<i>SERPINE2</i>	0.32991	0.08224	0.22788	0.00739
	<i>NFKBIZ</i>	0.45020	0.00000	-0.03879	0.58694
	<i>IER3</i>	0.95232	0.00006	-0.15880	0.34601
Macrophage	<i>CD74</i>	-1.48558	0.00011	-0.31001	0.15669
	<i>CD68</i>	-0.53701	0.09209	0.27243	0.00164
	<i>CCL3L1</i>	-0.71028	NA	0.49116	0.65090
	<i>HLA-DRB1</i>	-0.14499	0.83996	0.33236	0.42207
	<i>IL1B</i>	NA	NA	1.05518	0.11622
	<i>CXCL3</i>	-1.19083	0.03538	-0.34991	0.55653
	<i>LYZ</i>	-0.28907	NA	NA	NA
	<i>CXCL8</i>	-0.85258	0.00289	0.19976	0.49503
	<i>TYROBP</i>	-0.35837	NA	NA	NA
	<i>HLA-DPA1</i>	-0.84383	0.23701	1.14710	0.33285
Endothelial cell	<i>SPARCL1</i>	-0.84404	0.06955	-0.50420	0.26285
	<i>IFI27</i>	-0.63983	0.40687	1.53170	0.00732
	<i>PECAM1</i>	-0.35529	0.48922	-0.12910	0.73075
	<i>PLVAP</i>	-0.14245	0.84491	0.37112	0.36893
	<i>SYNE2</i>	-0.64702	0.00000	0.20163	0.03573
	<i>CALCRL</i>	0.10744	0.64821	0.42068	0.00639
	<i>IGFBP4</i>	-0.42947	0.00000	0.24125	0.00057
	<i>VWF</i>	-0.85639	0.00322	0.71970	0.02028
	<i>ITGA6</i>	-0.10931	0.48464	0.03303	0.79554
	<i>CD34</i>	-0.50161	0.16563	0.28226	0.44814

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Supplementary Table 2. Demographic data. A total of 11 subjects were recruited with an age between 13 – 71 (average = 34.2). Grade of disc degeneration was determined by MRI according to Pfirrmann criteria. F, female; M, male; IS, idiopathic scoliosis; IDD, intervertebral disc degeneration; ND, not determined.

Sample	Sex	Donor's Age (Years)	Level	Disease	Grade
1	F	13	L2-3	IS	ND
2	F	13	L2-3	IS	ND
3	M	15	L2-3	IS	ND
4	F	15	L2-3	IS	ND
5	F	16	L1-2	IS	ND
6	M	48	L4-L5	IDD	IV
7	M	40	L3-L4	IDD	III
8	F	42	L4-L5	IDD	IV
9	F	47	L3-L4	IDD	V
10	F	56	L4-L5	IDD	III
11	M	71	L4-L5	IDD	IV

Supplementary Table 3. Antibody information.

Description	Sources	Product Cat #
MMP12 Polyclonal Antibody	Invitrogen	PA5-13181
Elastin Polyclonal Antibody	Invitrogen	PA5-99418
Rabbit polyclonal to SOX9	Abcam	ab185230
LECT1 Polyclonal Antibody	Invitrogen	PA5-76974
Rabbit polyclonal to alpha smooth muscle Actin	Abcam	ab5694
Rabbit polyclonal to Fibroblast activation protein, alpha	Abcam	ab53066
Rabbit polyclonal to CYR61	Abcam	ab286129
Rabbit recombinant multiclonal [RM2036] to Aggrecan	Abcam	ab315486
Collagen I Polyclonal Antibody	Invitrogen	PA1-26204
Rabbit polyclonal to Collagen III	Abcam	ab7778
Collagen II Polyclonal Antibody	Invitrogen	PA5-99159
Rabbit polyclonal to GAPDH	Abcam	ab9485

132 **Supplementary Table 4. Primer sequences for RT-PCR.**

Gene ID		Sequence, 5'–3'
<i>ACTA2</i>	Sense	CTATGAGGGCTATGCCTTGCC
	Antisense	GCTCAGCAGTAGTAACGAAGGA
<i>COL1A1</i>	Sense	ATCAACCGGAGGAATTTCCGT
	Antisense	CACCAGGACGACCAGGTTTTC
<i>COL3A1</i>	Sense	TTGAAGGAGGATGTTCCCATCT
	Antisense	ACAGACACATATTTGGCATGGTT
<i>MMP12</i>	Sense	GGAATCCTAGCCCATGCTTTT
	Antisense	CATTACGGCCTTTGGATCACT
<i>TEK</i>	Sense	TCCGCTGGAAGTTACTCAAGA
	Antisense	GAACTCGCCCTTCACAGAAATAA
<i>KRT19</i>	Sense	ACCAAGTTTGAGACGGAACAG
	Antisense	CCCTCAGCGTACTGATTTCCT
<i>FAP</i>	Sense	CAAAGGCTGGAGCTAAGAATCC
	Antisense	ACTGCAAACATACTCGTTCATCA
<i>ITGB6</i>	Sense	TCCATCTGGAGTTGGCGAAAG
	Antisense	TCTGTCTGCCTACACTGAGAG
<i>CYR61</i>	Sense	CTCGCCTTAGTCGTCACCC
	Antisense	CGCCGAAGTTGCATTCCAG
<i>GAPDH</i>	Sense	GGAGCGAGATCCCTCCAAAAT
	Antisense	GGCTGTTGTCATACTTCTCATGG