Table1

Gene symbol	Higher in H than in PH zone		Higher in H than in PR zone	
	Fold change	*P*-value	Fold change	*P*-value
Agpat9	–	–	7.56	1.93E-08
Agpat9	–	–	6.45	1.87E-06
Ank	9.77	9.20E-09	5.11	2.62E-07
Arhgap24	3.21	7.62E-04	–	–
Bmp6	–	–	7.28	1.98E-07
Cd44	6.77	2.12E-06	5.12	3.73E-06
Cd44	5.07	3.85E-08	4.61	1.13E-07
Cdkn2b	–	–	4.16	6.59E-07
Dcn	3.08	3.29E-03	–	–
Ddit4l	–	–	27.37	3.32E-08
Ddit4l	–	–	13.19	1.77E-07
Ddit4l	–	–	8.63	3.94E-07
Dnajb9	–	–	3.31	4.55E-07
Dnajb9	–	–	5.02	2.08E-07
Fn1	3.64	1.29E-06	17.61	1.49E-05
Inhba	8.09	7.48E-07	15.83	8.09E-07
Jag1	11.73	1.83E-04	–	–
Kitl	4.48	1.35E-04	10.74	2.53E-04
Map1b	–	–	4.29	5.04E-07
Nr2f2	3.19	3.78E-04	4.10	1.68E-07
Nr2f2	4.16	7.94E-06	–	–
Pcdh17	4.01	2.30E-06	5.43	2.37E-06
Pdgfra	7.64	4.74E-07	3.31	5.09E-06
Pmepa1	4.38	3.02E-07	–	–
Ptgs2	13.26	2.62E-09	49.11	1.58E-09
Ptgs2	22.82	4.94E-10	187.12	9.16E-08
Rgcc	–	–	7.53	2.97E-08
Serpine1	–	–	10.13	1.67E-04
Slit2	3.74	4.87E-04	9.27	8.91E-04
Slit2	3.89	5.04E-07	18.03	2.96E-08
Smad7	–	–	6.94	1.52E-07
Timp3	–	–	7.09	1.36E-06
Tnnt2	–	–	3.82	1.65E-03
Gene symbol	Lower in H than in PH zone		Lower in H than in PR zone	
	Fold change	*P*-value	Fold change	*P*-value
Hhip	–	–	5.95	2.50E-08
Myrip	–	–	10.95	4.88E-07
Ncapg	–	–	4.37	3.82E-06
Ogn	3.43	5.50E-06	18.38	1.06E-08
Thbs4	5.23	1.12E-08	3.95	8.78E-08

Analyses based on Moderated T-test: Fold change ≥ 3 and P ≤ 0.01
– =not significantly regulated

Table2

Gene symbol	Higher in EC than in OI		Higher in EC than in II	
	Fold change	*P*-value	Fold change	*P*-value
6330415B21Rik	–	–	6.86	2.76E-04
Asb4	8.32	6.56E-04	9.01	7.42E-05
Bmp7	–	–	10.30	5.97E-03
Cdkn2b	–	–	3.32	4.66E-03
Dtna	–	–	3.83	3.23E-03
Gna14	–	–	7.52	7.55E-03
Ltbp1	–	–	3.22	7.46E-03
Papss2	3.96	3.84E-03	8.19	2.87E-05
Prkg2	6.58	2.49E-03	6.80	1.49E-04
Gene symbol	Lower in EC than in OI		Lower in EC than in II	
	Fold change	*P*-value	Fold change	*P*-value
Adamtsl2	5.06	6.00E-03	–	–
Ccnjl	–	–	7.43	1.30E-04
Gas6	–	–	4.87	7.24E-03
Hhip	3.92	9.55E-03	–	–
Hhip	11.52	1.94E-03	–	–
Scara3	3.97	5.17E-03	–	–
Thbs4	7.98	3.07E-04	23.66	6.33E-06
Wipf3	4.87	1.35E-03	–	–

Analyses based on Moderated T-test: Fold change ≥ 3 and P ≤ 0.01
– =not significantly regulated

Table3

Gene symbol	Gene name	Previously shown to be regulated in cartilage of animal model(s) for OA (early OA)	Previously shown to be regulated in human cartilage of patients with OA (late OA)
Adamtsl2	ADAMTS-like 2	–	Snelling, *et al.*, (2014)
Ankh	Progressive ankylosis	Du, *et al.*, (2016)	Hirose, *et al.*, (2002); Johnson, 2004; Sun, *et al.*, (2010a; 2010b); Wang, *et al.*, (2005)
Bmp6	Bone morphogenetic protein 6	–	Chou, *et al.*, (2013); Sanchez-Sabate, *et al.*, (2009)
Bmp7	Bone morphogenetic protein 7	–	Bhutia, *et al.*, (2014); Bobinac, *et al.*, (2008); Chubinskaya, *et al.*, (2000); Merrihew, *et al.*, (2003); Schmal, *et al.*, (2015)
Cd44	CD44 antigen	Rao, *et al.*, (2014); Tibesku, *et al.*, (2005)	Dunn, *et al.*, (2009); Fuchs, *et al.*, (2003); Ostergaard, *et al.*, (1997); Zhang, *et al.*, (2013)
Dcn	Decorin	Adams, *et al.*, (1995); Young, *et al.*, (2002; 2005)	Bock, *et al.*, (2001); Cs-Szabo, *et al.*, (1995); Dourado, *et al.*, (1996); Little, *et al.*, (1996); Liu, *et al.*, (2003); Masse, *et al.*, (1997); Melrose, *et al.*, (2008); Poole, *et al.*, (1996)
Fn1	Fibronectin 1	Burton-Wurster, *et al.*, (1985; 1986; 1988); Chang, *et al.*(2017); Gardiner, *et al.*, (2015); Sandya, *et al.*, (2007); Wurster and Lust, (1984); Zang, *et al.*, (1995)	Aigner, *et al.*, (2001); Carnemolla, *et al.*, (1984); Chevalier, *et al.*, (1992; 1996); Dunn, *et al.*, (2016); Gardiner, *et al.*, (2015); Homandberg, *et al.*, (1998); Jones, *et al.*, (1987); Lorenzo, *et al.*, (2004); Miller, *et al.*, (1984); Parker, *et al.*, (2002); Wright, *et al.*, (1996); Zack, *et al.*, (2006)
Hhip	Hedgehog interacting protein	Shuang, *et al.*, (2015)	–
Inhba	Inhibin beta A subunit	Wei, *et al.*, (2010)	Hopwood, *et al.*, (2007); Wei, *et al.*, (2010)
Jag1	Jagged 1	Gardiner, *et al.*, (2015); Hosaka, *et al.*, (2013)	Gardiner, *et al.*, (2015); Karlsson, *et al.*, (2008); Sassi, *et al.*, (2014)
Kitlg	KIT ligand	Appleton, *et al.*, (2007)	Ceponis, *et al.*, (1998)
Ogn	Osteoglycin	–	Chou, *et al.*, (2013); Juchtmans, *et al.*, (2015); Wang, *et al.*, (2016)
Papss2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	Ford-Hutchinson, *et al.*, (2005)	Ikeda, *et al.*, (2001); Luo, *et al.*, (2014)
Ptgs2	Prostaglandin-endoperoxide synthase 2	Appleton, *et al.*, (2007); Dumond, *et al.*, (2004); Fukai, *et al.*, (2012); Le Graverand, *et al.*, (2001)	Amin, *et al.*, (1997); Casagrande, *et al.*, (2015); Fan, *et al.*, (2015); Fukai, *et al.*, (2012); Koki, *et al.*, (2002); Valdes, *et al.*, (2004; 2006; 2008)
Rgcc	Regulator of cell cycle	–	Tew, *et al.*, (2007)
Serpine1	Serpin family E member 1	Bao, *et al.*, (2009); Le Graverand, *et al.*, (2001)	Belcher, *et al.*, (1996); Cevidanes, *et al.*, (2014); Franses, *et al.*, (2010); Martel-Pelletier, *et al.*, (1991)
Smad7	SMAD family member 7	–	Kaiser, *et al.*, (2004);
Timp3	Tissue inhibitor of metalloproteinase 3	–	Casagrande, *et al.*, (2015); Franses, *et al.*, (2010); Gardiner, *et al.*, (2015); Kevorkian, *et al.*, (2004); Li, *et al.*, (2014); Morris, *et al.*, (2010); Sahebjam, *et al.*, (2007); Su, *et al.*, (2015)

Table4

Gene symbol	Gene name	Knockout mice have skeletal phenotype?	Regulated in human OA cartilage?
Ltbp1	Latent transforming growth factor beta binding protein 1	Yes [49]	Yes [53, 58]
Nr2f2	Nuclear receptor subfamily 2 group F member 2	Yes [50]	Yes [56, 57]
Pdgfra	Platelet derived growth factor receptor alpha	Yes [51]	Yes [59]
Prkg2	Protein kinase, cGMP-dependent, type II	Yes [52]	Yes [57]
Pmepa1	Prostate transmembrane protein, androgen induced 1	No data available	Yes [54-56]
Ddit4l	DNA damage inducible transcript 4 like	No data available	Yes [53, 55]
Scara3	Scavenger receptor class A member 3	No data available	Yes [53, 55]
Ncapg	Non-SMC condensin I complex subunit G	No data available	Yes [57]
Thbs4	Thrombospondin 4	No	Yes [54, 57]
Map1b	Microtubule associated protein 1B	No	Yes [53, 57]
Agpat9	Glycerol-3-phosphate acyltransferase 3	No	Yes [57]
Arhgap24	Rho GTPase activating protein 24	No	Yes [57]
Cdkn2b	Cyclin dependent kinase inhibitor 2B	No	Yes [57]
Dnajb9	DnaJ heat shock protein family (Hsp40) member B9	No	Yes [56]
Gas6	Growth arrest specific 6	No	Yes [56]
Ccnjl	Cyclin J like	No data available	No
Myrip	Myosin VIIA and Rab interacting protein	No data available	No
6330415B21Rik	-	No data available	No
Gna14	G protein subunit alpha 14	No data available	No
Asb4	Ankyrin repeat and SOCS box containing 4	No	No
Dtna	Dystrobrevin alpha	No	No
Pcdh17	Protocadherin 17	No	No
Slit2	Slit guidance ligand 2	No	No
Tnnt2	Troponin T2, cardiac type	No	No
Wipf3	WAS/WASL interacting protein family member 3	No	No

Table 4: TGFβ-related genes that have not been previously implicated in OA. The 25 TGFβ-related genes that have not been previously associated with OA were further studied in literature to obtain indications for a potential role in skeletal tissue development and homeostasis. Moreover, it was evaluated whether these genes were regulated in human OA cartilage using published microarray studies.

Figure1
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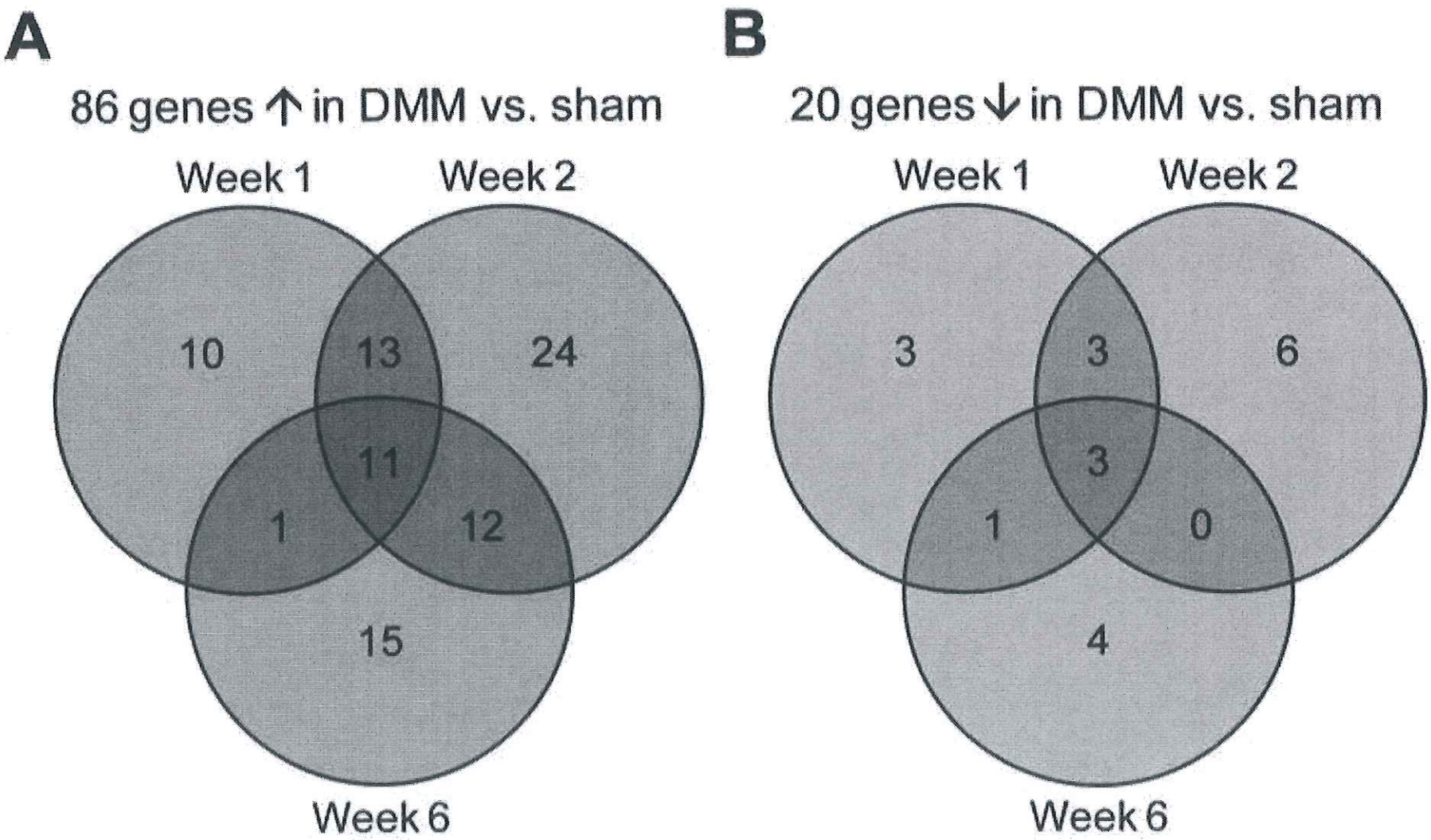

Figure2
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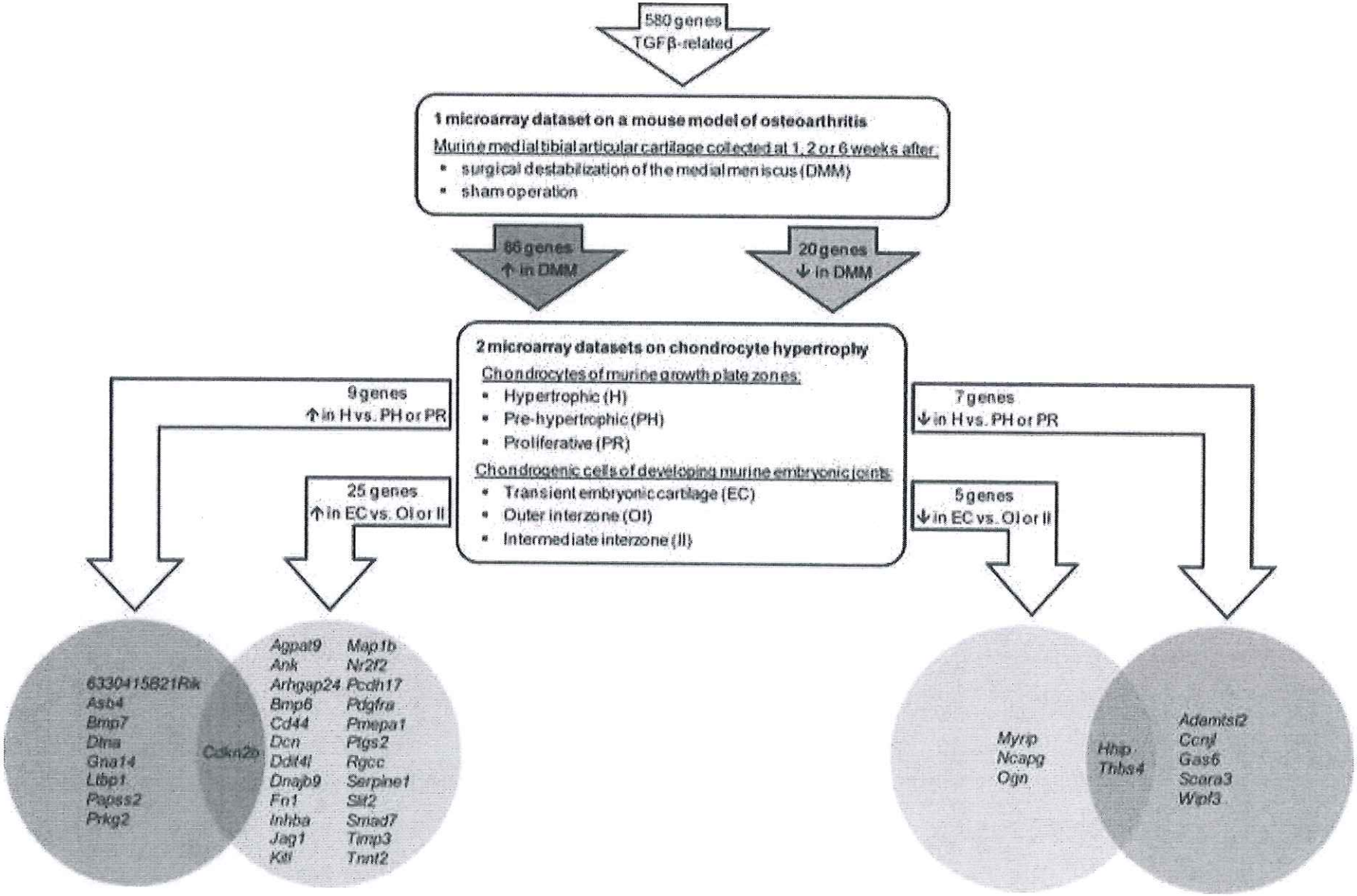
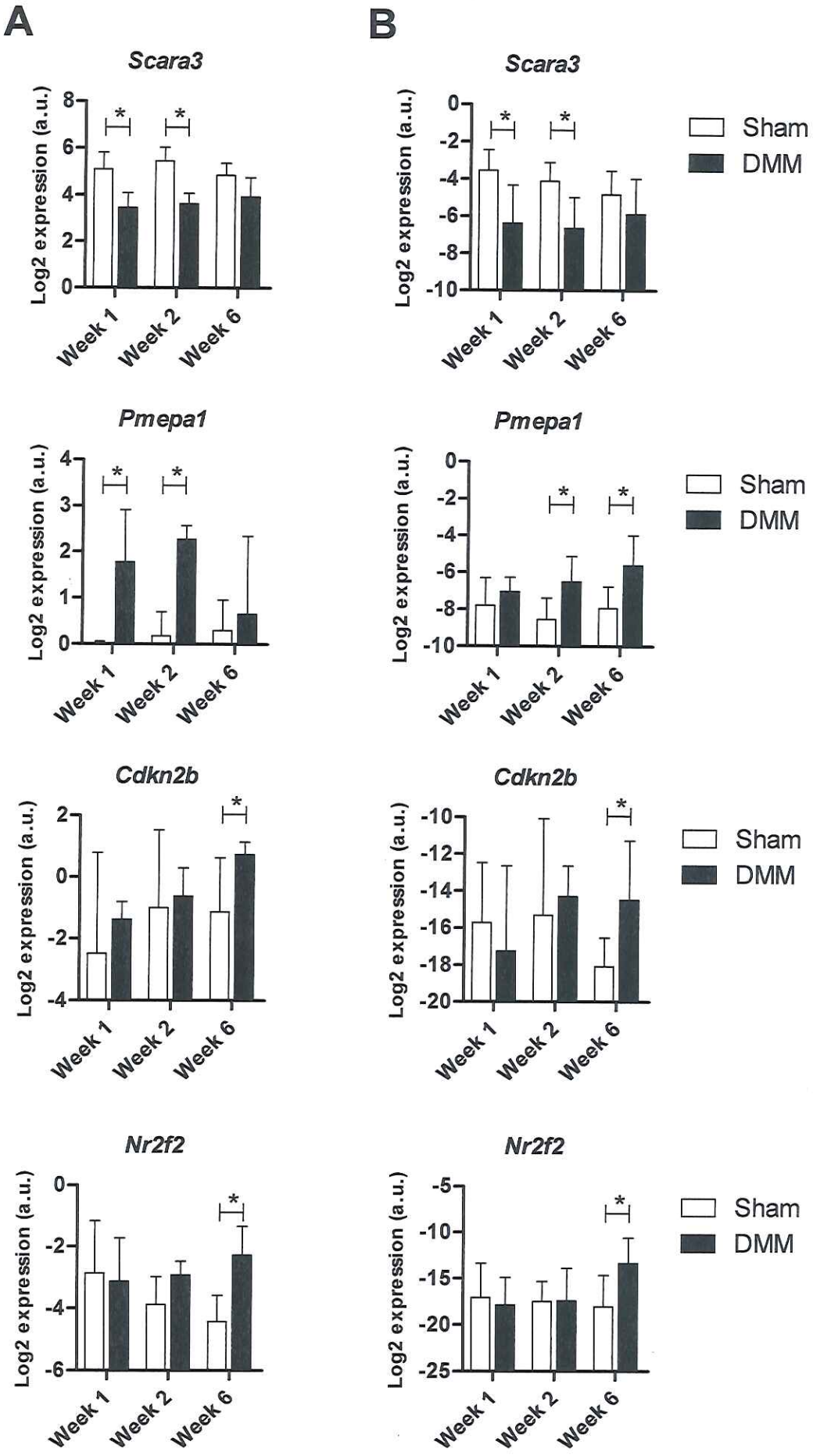


Figure3


A
B
Scara3
Pmepa1
Cdkn2b
Nr2f2
Log2 expression (a.u.)
Week 1
Week 2
Week 6
Sham
DMM
*