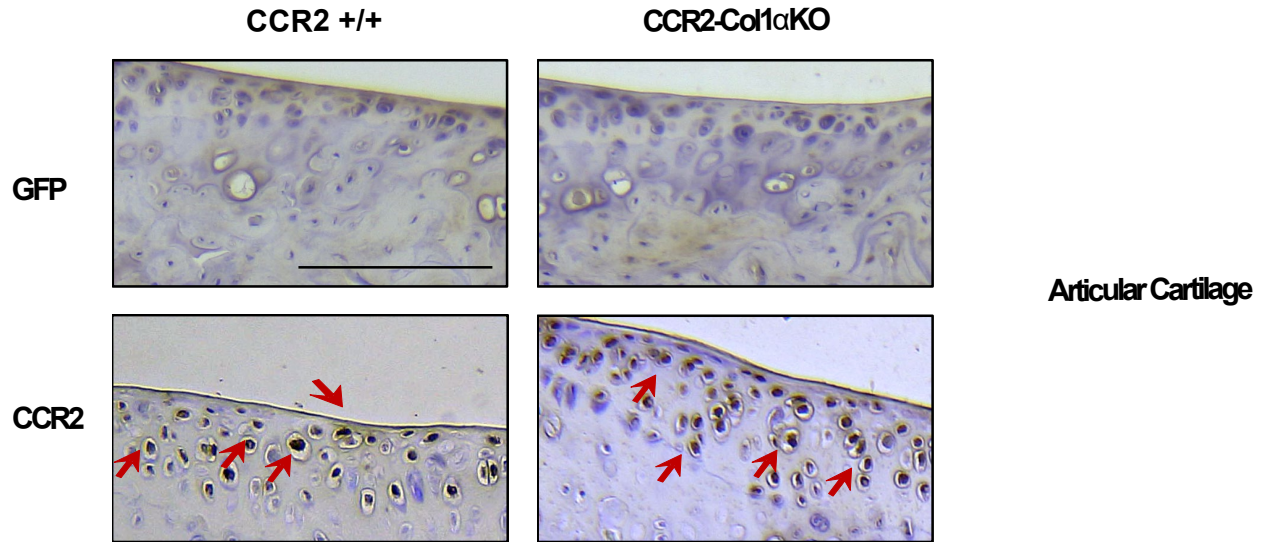
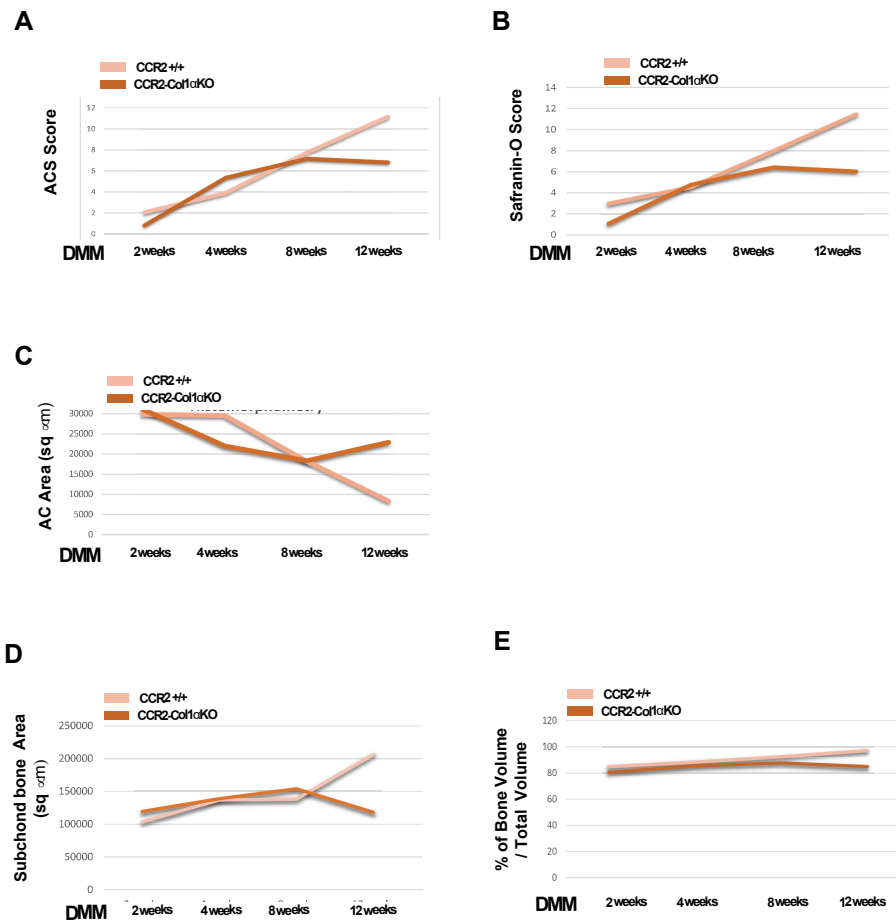


## SUPPLEMENTAL FIGURES

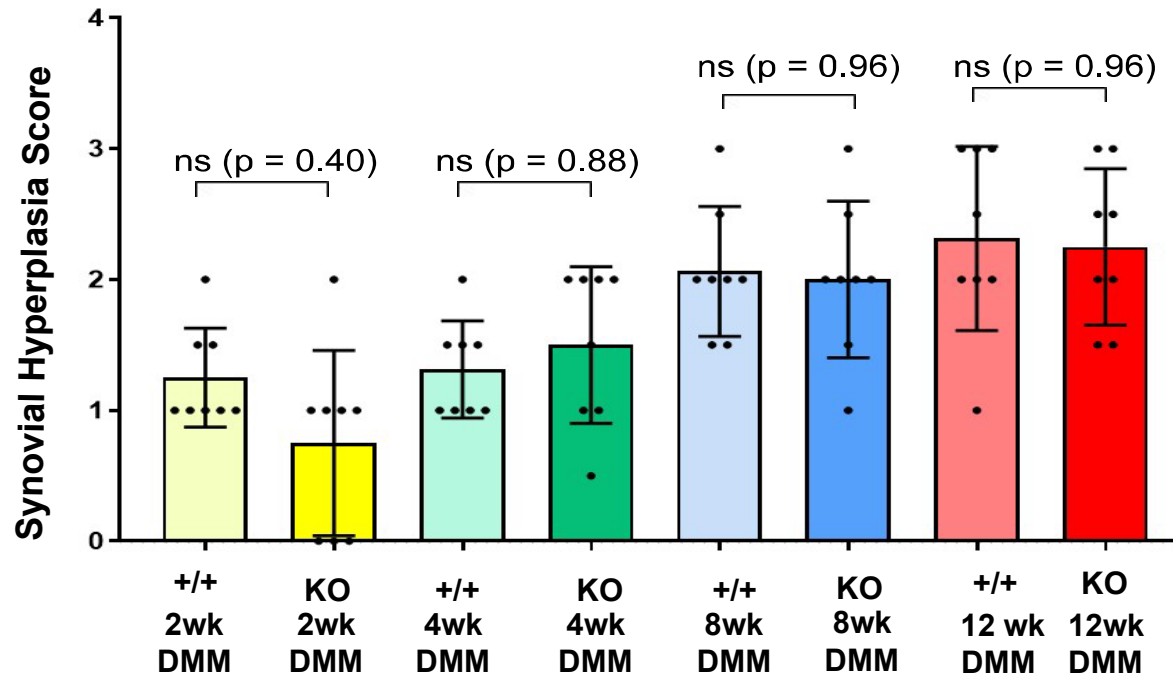


**Supplemental Figure S1**

**Supplemental Figure S1. Protein levels of CCR2 and GFP in the articular cartilage (AC) of *CCR2-Col1αKO* and *CCR2+/+* mice following Tamoxifen injection.** Paraffin embedded knee joint sections are immunostained for GFP and CCR2, two weeks after the first Tam injection. Positive staining is detected as brown precipitate (red arrows). GFP staining is not detected in any of the genotypes. Conversely, CCR2 staining is detected in the AC cells of both *CCR2+/+* and *CCR2-Col1αKO* mice. Images are representative of 6 different mice for each of the experimental groups described, ranging between 14 and 18 weeks of age. Scale bars are 100  $\mu\text{m}$ .

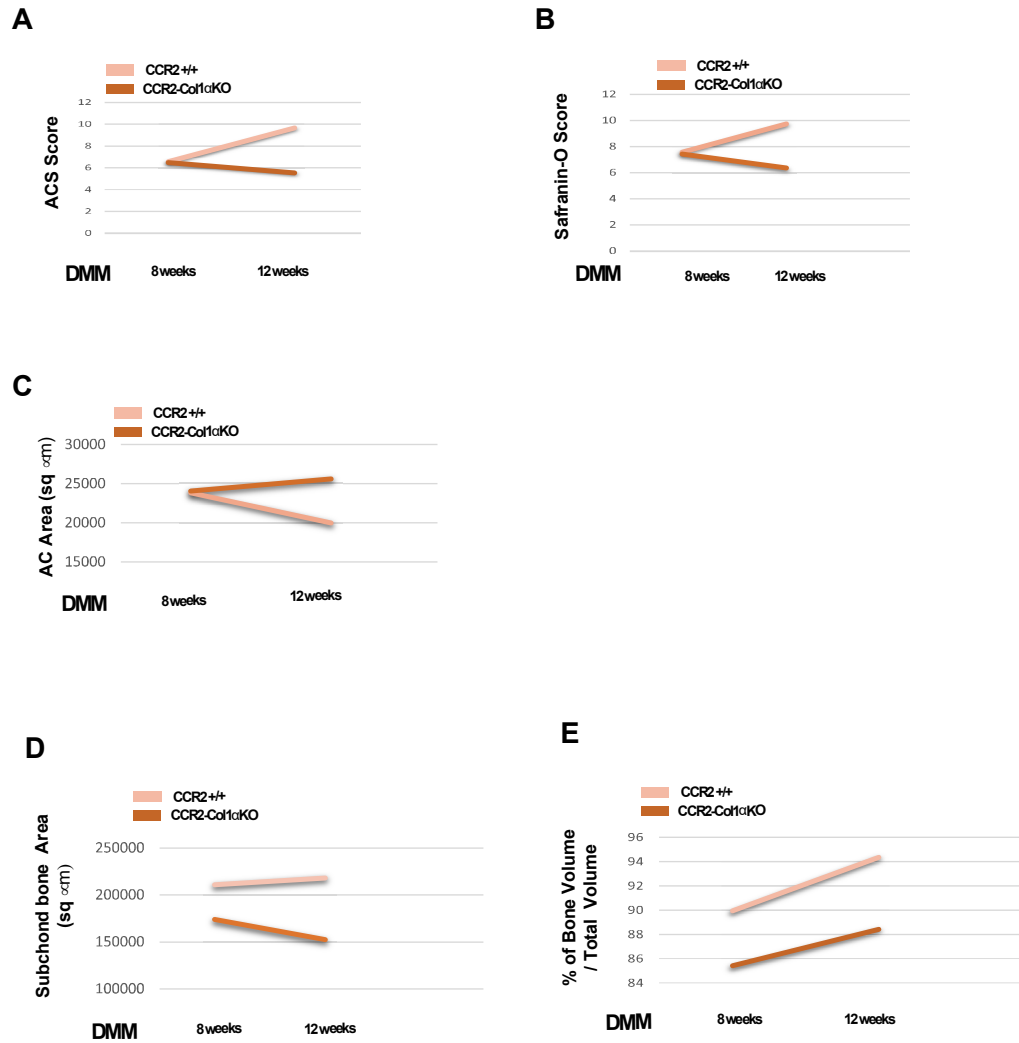


**Supplemental Figure S2.** PTOA assessment in mouse knee joints of *CCR2-Col1a*KO and *CCR2*<sup>+/+</sup> within each genotype, following early *Ccr2* inactivation. ACS, Saf-O score, Histomorphometric analysis of cartilage quantification, Subchondral bone thickness and percentabe of bone volume / Total Volume (BV/TV) were assessed at the time point indicated following early *Ccr2* inactivation (before DMM). N=8 mice for each experimental point. Within each genotype (*CCR2*<sup>+/+</sup>, light orange; *CCR2-Col1a*KO, dark orange), group analyses were performed with ordinary one-way ANOVA, followed by Tukey's post-hoc test for multiple comparisons, available in the [Supplemental Table S1](#).



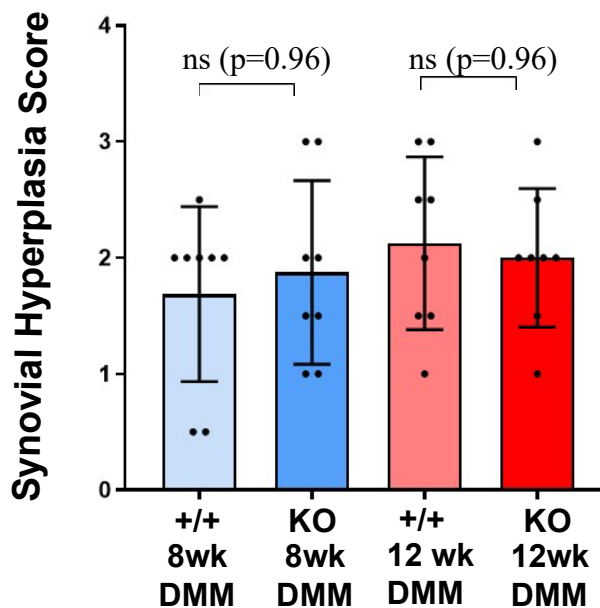
**Supplemental Figure S3**

**Supplemental Figure S3.** Synovial hyperplasia assessment in mouse knee joints of *CCR2-Col1αKO* and *CCR2+/+*, following early CCR2 inactivation. Synovial hyperplasia scores (scale 0-3) of *CCR2-Col1αKO* and *CCR2+/+* mouse knees at the time point indicated. *N*=8 mice for each experimental point. The graphs represents the mean  $\pm$  standard deviation; indicated *P*-values were determined by Wilcoxon rank sum tests at each time point, following adjustment for multiple comparisons.



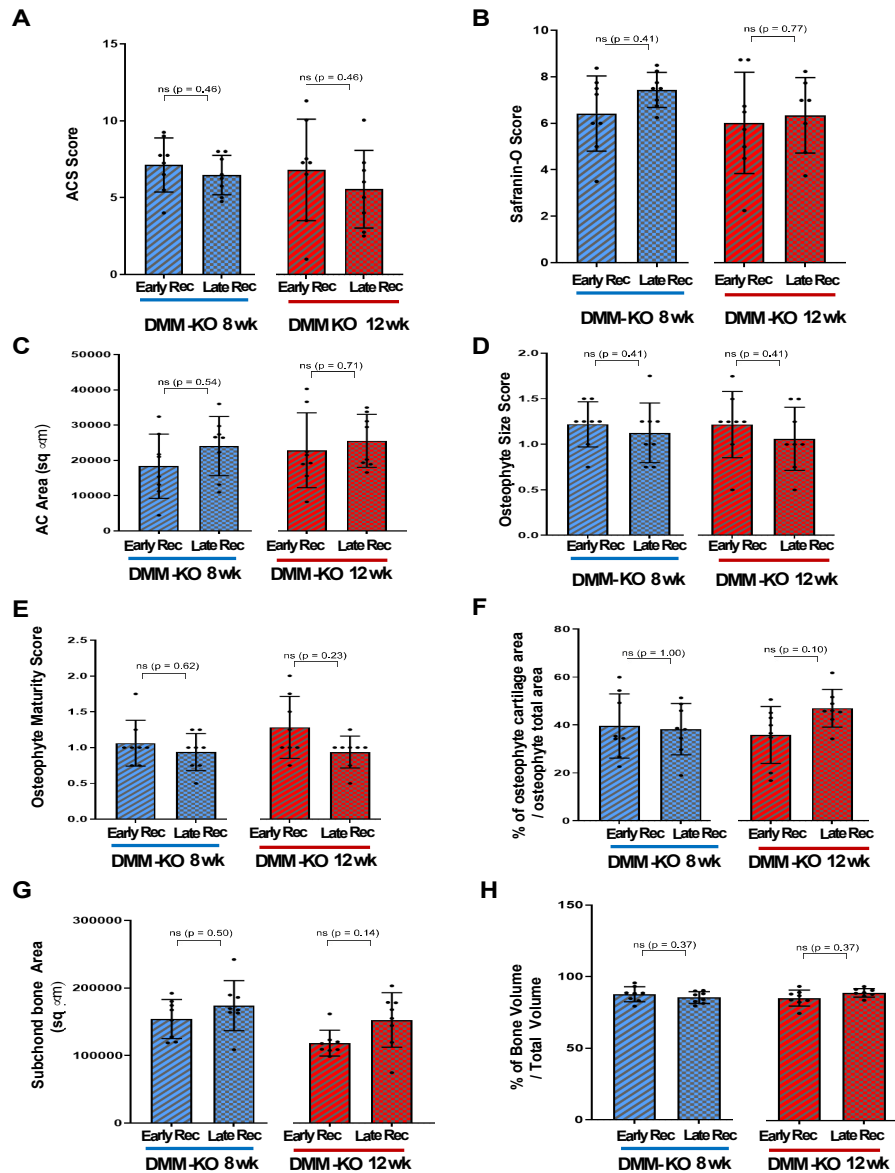
**Supplemental Figure S4**

**Supplemental Figure S4.** PTOA assessment in mouse knee joints of *CCR2-Col1αKO* and *CCR2+/+* within each genotype, following late *Ccr2* inactivation. ACS, Saf-O score, Histomorphometric analysis of cartilage quantification, Subchondral bone thickness and percentabe of bone volume / Total Volume (BV/TV) were assessed at the time point indicated following late *Ccr2* inactivation (at 4 weeks after DMM). *N*=8 mice for each experimental point. Within each genotype (*CCR2+/+* , light orange; *CCR2-Col1αKO*, dark orange), group analyses were performed with Welch's t-test, available in the [Supplemental Table S3](#).



### Supplemental Figure S5

**Supplemental Figure S5.** Synovial hyperplasia assessment in mouse knee joints of *CCR2-Col1αKO* and *CCR2+/+*, following late *CCR2* inactivation. Synovial hyperplasia scores (scale 0-3) of *CCR2-Col1αKO* and *CCR2+/+* mouse knees at the time point indicated. *N*=8 mice for each experimental point. The graphs represents the mean  $\pm$  standard deviation; indicated p-values were determined by Wilcoxon rank sum tests at each time point, following adjustment for multiple comparisons.



Supplemental Figure S6

**Supplemental Figure S6.** PTOA assessment in mouse knee joints of *CCR2-Col1aKO* comparing early vs late *Ccr2* ablation. ACS, Saf-O score, Histomorphometric analysis of cartilage quantification, Osteophyte Size, Osteophyte maturity, Osteophyte cartilage quantification, Subchondral bone thickness and percentage of bone volume / Total Volume (BV/TV) were compared at 8 and 12 weeks after DMM.  $N=8$  mice for each experimental point. The graphs represent the mean  $\pm$  standard deviation; indicated p-values were determined by Wilcoxon rank sum tests at each time point, following adjustment for multiple comparisons, available in the Supplemental Table S7.

# SUPPLEMENTAL TABLES

OA Parameter Early Recomb.	Groups	Mean Diff.	95.00% CI of diff.	Adjusted <i>P</i> -value
<b>ACS</b>	DMM 2w CCR2 +/+ vs. DMM 4w CCR2 +/+	-1.844	-3.100 to -0.5877	<b>0.0022</b>
	DMM 2w CCR2 +/+ vs. DMM 8w CCR2 +/+	-5.688	-6.944 to -4.431	<b>&lt;0.0001</b>
	DMM 2w CCR2 +/+ vs. DMM 12w CCR2 +/+	-9.094	-10.35 to -7.838	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 8w CCR2 +/+	-3.844	-5.100 to -2.588	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 12w CCR2 +/+	-7.25	-8.506 to -5.994	<b>&lt;0.0001</b>
	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-3.406	-4.662 to -2.150	<b>&lt;0.0001</b>
<b>Saf-O</b>	DMM 2w CCR2 +/+ vs. DMM 4w CCR2 +/+	-1.563	-2.960 to -0.1650	<b>0.024</b>
	DMM 2w CCR2 +/+ vs. DMM 8w CCR2 +/+	-5	-6.398 to -3.602	<b>&lt;0.0001</b>
	DMM 2w CCR2 +/+ vs. DMM 12w CCR2 +/+	-8.5	-9.898 to -7.102	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 8w CCR2 +/+	-3.438	-4.835 to -2.040	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 12w CCR2 +/+	-6.938	-8.335 to -5.540	<b>&lt;0.0001</b>
	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-3.5	-4.898 to -2.102	<b>&lt;0.0001</b>
<b>Cartilage Histomorph.</b>	DMM 2w CCR2 +/+ vs. DMM 4w CCR2 +/+	265.8	-7257 to 7789	0.9997
	DMM 2w CCR2 +/+ vs. DMM 8w CCR2 +/+	11657	4134 to 19180	<b>0.0012</b>
	DMM 2w CCR2 +/+ vs. DMM 12w CCR2 +/+	21449	13926 to 28972	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 8w CCR2 +/+	11391	3868 to 18914	<b>0.0016</b>
	DMM 4w CCR2 +/+ vs. DMM 12w CCR2 +/+	21183	13660 to 28706	<b>&lt;0.0001</b>
	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	9792	2269 to 17315	<b>0.0071</b>
<b>Subchondral Bone Thickness</b>	DMM 2w CCR2 +/+ vs. DMM 4w CCR2 +/+	-33145	-75391 to 9101	0.1647
	DMM 2w CCR2 +/+ vs. DMM 8w CCR2 +/+	-34614	-76860 to 7633	0.138
	DMM 2w CCR2 +/+ vs. DMM 12w CCR2 +/+	-102378	-144624 to -60132	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 8w CCR2 +/+	-1469	-43715 to 40778	0.9997
	DMM 4w CCR2 +/+ vs. DMM 12w CCR2 +/+	-69233	-111479 to -26986	<b>0.0006</b>
	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-67764	-110010 to -25518	<b>0.0008</b>
<b>% BV/TV</b>	DMM 2w CCR2 +/+ vs. DMM 4w CCR2 +/+	-3.402	-8.930 to 2.126	0.3526
	DMM 2w CCR2 +/+ vs. DMM 8w CCR2 +/+	-7.509	-13.04 to -1.981	<b>0.0048</b>
	DMM 2w CCR2 +/+ vs. DMM 12w CCR2 +/+	-12.3	-17.83 to -6.770	<b>&lt;0.0001</b>
	DMM 4w CCR2 +/+ vs. DMM 8w CCR2 +/+	-4.107	-9.635 to 1.421	0.2019
	DMM 4w CCR2 +/+ vs. DMM 12w CCR2 +/+	-8.896	-14.42 to -3.368	<b>0.0008</b>
	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-4.789	-10.32 to 0.7389	0.1075

OA Parameter Early Recomb.	Groups	Mean Diff.	95.00% CI of diff.	Adjusted <i>P</i> -value
<b>ACS</b>	DMM 2w CCr2-Col1KO vs. DMM 4w CCr2-Col1KO	-4.531	-7.259 to -1.804	<b>0.0005</b>
	DMM 2w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-6.313	-9.040 to -3.585	<b>&lt;0.0001</b>
	DMM 2w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-5.969	-8.696 to -3.241	<b>&lt;0.0001</b>
	DMM 4w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-1.781	-4.509 to 0.9462	0.3023
	DMM 4w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-1.438	-4.165 to 1.290	0.4866
	DMM 8w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	0.3438	-2.384 to 3.071	0.9857
<b>Saf-O</b>	DMM 2w CCr2-Col1KO vs. DMM 4w CCr2-Col1KO	-3.688	-5.725 to -1.650	<b>0.0002</b>
	DMM 2w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-5.359	-7.397 to -3.322	<b>&lt;0.0001</b>
	DMM 2w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-4.969	-7.006 to -2.931	<b>&lt;0.0001</b>
	DMM 4w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-1.672	-3.709 to 0.3655	0.1371
	DMM 4w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-1.281	-3.319 to 0.7561	0.3341
	DMM 8w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	0.3906	-1.647 to 2.428	0.9527
<b>Cartilage Histomorph.</b>	DMM 2w CCr2-Col1KO vs. DMM 4w CCr2-Col1KO	9081	-2274 to 20436	0.1526
	DMM 2w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	12709	1353 to 24064	<b>0.0238</b>
	DMM 2w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	8136	-3220 to 19491	0.2286
	DMM 4w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	3628	-7727 to 14983	0.819
	DMM 4w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-945.3	-12300 to 10410	0.9958
	DMM 8w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-4573	-15928 to 6782	0.6927
<b>Subchondral Bone Thickness</b>	DMM 2w CCr2-Col1KO vs. DMM 4w CCr2-Col1KO	-19020	-64918 to 26877	0.6736
	DMM 2w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-34376	-80273 to 11522	0.1961
	DMM 2w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	1646	-44252 to 47543	0.9997
	DMM 4w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-15356	-61253 to 30542	0.7979
	DMM 4w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	20666	-25232 to 66563	0.6139
	DMM 8w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	36021	-9876 to 81919	0.1645
<b>% BV/TV</b>	DMM 2w CCr2-Col1KO vs. DMM 4w CCr2-Col1KO	-5.039	-12.41 to 2.331	0.2649
	DMM 2w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-7.175	-14.55 to 0.1953	0.0585
	DMM 2w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	-4.313	-11.68 to 3.057	0.3961
	DMM 4w CCr2-Col1KO vs. DMM 8w CCr2-Col1KO	-2.136	-9.506 to 5.235	0.8578
	DMM 4w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	0.7263	-6.644 to 8.097	0.993
	DMM 8w CCr2-Col1KO vs. DMM 12w CCr2-Col1KO	2.862	-4.508 to 10.23	0.716

**Supplemental Table S1.** PTOA assessment in mouse knee joints of *CCR2-Col1aKO* and *CCR2+/+* within each genotype, following early *Ccr2* inactivation.

Within each genotype (*CCR2+/+* or *CCR2-Col1aKO*, group analyses were performed with ordinary one-way ANOVA, followed by Tukey's post-hoc test for multiple comparisons.



**Supplemental Table S2.** Effect of early CCR2 inactivation (before DMM) on synovial hyperplasia in mouse CCR2-Col1 $\alpha$ KO and CCR2+/+ knee joints (N=8).

OA Parameters		Week 2				Week 4			
		Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)	Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)
Synovial Hyperplasia	DMM CCR2+/+	1.63(0.40)	10.31	1	1.25(0.38)	-0.77 [0.88]	7.56	1.25	1.31(0.37)
	DMM CCR2-AggKO		6.69	1	0.75(0.71)		9.44	1.75	1.50(0.60)

OA Parameters		Week 8				Week 12			
		Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)	Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)
Synovial Hyperplasia	DMM CCR2+/+	0.06(0.96)	8.63	2	2.06(0.50)	0.27(0.96)	8.88	2.25	2.31(0.70)
	DMM CCR2-AggKO		8.38	2	2.00(0.60)		8.13	2.25	2.25(0.60)

Data presented show median, mean and standard deviation (SD), for each group at separate time points (2, 4, 8 and 12 weeks post-surgery). Indicated z- and P-values were determined by Wilcoxon rank sum tests between DMM CCR2+/+ and DMM CCR2-Col1 $\alpha$ KO groups separately at each time point, following adjustment for multiple comparison (Benjamini-Hochberg).

**Supplemental Table S3.** PTOA assessment in mouse knee joints of *CCR2-Col1aKO* and *CCR2+/+* within each genotype, following late *Ccr2* inactivation.

OA Parameter Late Recomb.	Groups	Mean Diff.	95.00% CI of diff.	P-value
<b>ACS</b>	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-3.09	-5.45, -0.74	<b>0.001</b>
<b>Saf-O</b>	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-2.19	-5.04, 0.664	0.12
<b>Cartilage Histomorph.</b>	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	3833	-4852, 12518	0.34
<b>Subchondral Bone Thickness</b>	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-7521	-54862, 39821	0.74
<b>% BV/TV</b>	DMM 8w CCR2 +/+ vs. DMM 12w CCR2 +/+	-4.41	-9.41, 0.60	0.08

OA Parameter Late Recomb.	Groups	Mean Diff.	95.00% CI of diff.	P-value
<b>ACS</b>	DMM 8w CCR2-Col1KO vs. DMM 12w CCR2-Col1KO	0.94	-1.27, 3.15	0.37
<b>Saf-O</b>	DMM 8w CCR2-Col1KO vs. DMM 12w CCR2-Col1KO	1.08	-0.46, 2.62	0.14
<b>Cartilage Histomorph.</b>	DMM 8w CCR2-Col1KO vs. DMM 12w CCR2-Col1KO	-1554	-10110, 7002	0.7
<b>Subchondral Bone Thickness</b>	DMM 8w CCR2-Col1KO vs. DMM 12w CCR2-Col1KO	21555	-19894, 63005	0.28
<b>% BV/TV</b>	DMM 8w CCR2-Col1KO vs. DMM 12w CCR2-Col1KO	-3.008	-6.87, 0.85	0.12

Within each genotype (*CCR2+/+* or *CCR2-Col1aKO*) group analyses were performed with the original data with Welch's t-test.

**Supplemental Table S4.** Effect of late CCR2 inactivation (4 weeks post-DMM) on synovial hyperplasia in mouse CCR2-Col1 $\alpha$ KO and CCR2+/+ knee joint (N=8).

OA Parameters		Week 8				Week 12			
		Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)	Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)
Synovial Hyperplasia	CCR2+/+	-0.06 [0.96]	8.38	2	1.69(0.75)	0.32 [0.96]	8.94	2.25	2.13(0.74)
	CCR2- <i>AggKO</i>		8.63	1.75	1.88(0.79)		8.06	2	2.0(0.58)

Data presented show median, mean and standard deviation (SD), for each group at separate time points (8 and 12 weeks post-surgery). Indicated z- and P-values were determined by Wilcoxon rank sum tests between DMM CCR2+/+ and DMM CCR2-Col1 $\alpha$ KO groups separately at each time point, following adjustment for multiple comparison (Benjamini-Hochberg).

**Supplemental Table S5. LMM results for incapacitance meter scores.** Estimated difference between groups, Standard Error, Adjusted P-values and lower and upper 95% confidence limits (LCL and UCL). Significant *P*-values ( $\leq 0.05$ ) are indicated in bold.

Time point	Group 1	Group 2	Estimate	Standard Error	Adj P	Adj Lower	Adj Upper
4 weeks	DMM CCR2+/+	DMM CCR2-Col1KO	0.008247	0.02542	0.748	-0.04381	0.06031
	SHAM CCR2 +/+	SHAM CCR2-Col1 KO	0.02815	0.03077	0.3682	-0.03489	0.09118
	DMM CCR2+/+	SHAM CCR2+/+	-0.03526	0.02788	0.2163	-0.09236	0.02184
	DMM CCR2-Col1KO	SHAM CCR2-Col1KO	-0.01536	0.02856	0.5949	-0.07387	0.04315
8 weeks	DMM CCR2+/+	DMM CCR2-Col1KO	0.143	0.05671	<b>0.0177</b>	0.02683	0.2592
	SHAM CCR2 +/+	SHAM CCR2-Col1 KO	0.04836	0.06867	0.4871	-0.0923	0.189
	DMM CCR2+/+	SHAM CCR2+/+	0.07648	0.0622	0.2291	-0.05093	0.2039
	DMM CCR2-Col1KO	SHAM CCR2-Col1KO	-0.01815	0.06374	0.778	-0.1487	0.1124
12 weeks	DMM CCR2+/+	DMM CCR2-Col1KO	0.06495	0.03787	0.0974	-0.01262	0.1425
	SHAM CCR2 +/+	SHAM CCR2-Col1 KO	0.02656	0.04617	0.5697	-0.06802	0.1211
	DMM CCR2+/+	SHAM CCR2+/+	0.06594	0.04205	0.1281	-0.02019	0.1521
	DMM CCR2-Col1KO	SHAM CCR2-Col1KO	0.02755	0.04241	0.5213	-0.05932	0.1144
16 weeks	DMM CCR2+/+	DMM CCR2-Col1KO	0.1472	0.05303	<b>0.0097</b>	0.03852	0.2558
	SHAM CCR2 +/+	SHAM CCR2-Col1 KO	-0.02212	0.06526	0.7371	-0.1558	0.1116
	DMM CCR2+/+	SHAM CCR2+/+	0.1305	0.05681	<b>0.0293</b>	0.01414	0.2469
	DMM CCR2-Col1KO	SHAM CCR2-Col1KO	-0.03878	0.062	0.5367	-0.1658	0.08823
20 weeks	DMM CCR2+/+	DMM CCR2-Col1KO	0.1576	0.04078	<b>0.0006</b>	0.07406	0.2411
	SHAM CCR2 +/+	SHAM CCR2-Col1 KO	0.01435	0.0483	0.7686	-0.08459	0.1133
	DMM CCR2+/+	SHAM CCR2+/+	0.1348	0.04375	<b>0.0046</b>	0.04523	0.2245
	DMM CCR2-AggKO	SHAM CCR2-Col1KO	-0.0084	0.04563	0.8552	-0.1019	0.08506

**Supplemental Table S6. Between-group mean differences in Von Frey Analyses and 95% CIs.**

Results are least-squares mean differences [ESTIMATED MEAN in GROUP1 – ESTIMATED MEAN in GROUP2] and corresponding 95% confidence intervals from linear mixed effects model. Significant *P*-values ( $\leq 0.05$ ) are indicated in bold.

Time point	Group1	Group2	DIFF_CI_BT	<i>P</i> -value
4 weeks	Contral. CCR2 +/+	DMM CCR2+/+	-0.04 (-0.64,0.56)	0.913167017
	Contral. CCR2 +/+	Contral. CCR2-Col1KO	-0.14 (-0.78,0.5)	0.683122675
	Contral. CCR2 +/+	DMM CCR2-Col1KO	-0.37 (-1.07,0.33)	0.306611043
	DMM CCR2+/+	Contral. CCR2-Col1KO	-0.1 (-0.74,0.54)	0.765285234
	DMM CCR2+/+	DMM CCR2-Col1KO	-0.33 (-1.03,0.37)	0.361282828
	Contral. CCR2-Col1KO	DMM CCR2-Col1KO	-0.23 (-0.91,0.45)	0.519439593
8 weeks	Contral. CCR2 +/+	DMM CCR2+/+	-0.02 (-0.64,0.59)	0.945546013
	Contral. CCR2 +/+	Contral. CCR2-Col1KO	0 (-0.62,0.62)	0.998408783
	Contral. CCR2 +/+	DMM CCR2-Col1KO	-0.21 (-0.9,0.48)	0.564371959
	DMM CCR2+/+	Contral. CCR2-Col1KO	0.02 (-0.6,0.65)	0.947672025
	DMM CCR2+/+	DMM CCR2-Col1KO	-0.19 (-0.88,0.51)	0.610903109
	Contral. CCR2-Col1KO	DMM CCR2-Col1KO	-0.21 (-0.88,0.46)	0.552282224
12 weeks	Contral. CCR2 +/+	DMM CCR2+/+	0.66 (0.19,1.14)	<b>0.006357264</b>
	Contral. CCR2 +/+	Contral. CCR2-Col1KO	0.2 (-0.34,0.73)	0.47920658
	Contral. CCR2 +/+	DMM CCR2-Col1KO	0.2 (-0.33,0.73)	0.472760071
	DMM CCR2+/+	Contral. CCR2-Col1KO	-0.47 (-0.96,0.02)	0.061238969
	DMM CCR2+/+	DMM CCR2-Col1KO	-0.46 (-0.95,0.03)	0.062683876
	Contral. CCR2-Col1KO	DMM CCR2-Col1KO	0 (-0.45,0.45)	0.991157927
16 weeks	Contral. CCR2 +/+	DMM CCR2+/+	0.44 (0.02,0.86)	<b>0.037585934</b>
	Contral. CCR2 +/+	Contral. CCR2-Col1KO	-0.07 (-0.52,0.39)	0.790616054
	Contral. CCR2 +/+	DMM CCR2-Col1KO	0.42 (-0.03,0.87)	0.064456736
	DMM CCR2+/+	Contral. CCR2-Col1KO	-0.51 (-0.96,-0.05)	0.027903491
	DMM CCR2+/+	DMM CCR2-Col1KO	-0.02 (-0.4,0.36)	0.930101194
	Contral. CCR2-Col1KO	DMM CCR2-Col1KO	0.49 (0.07,0.91)	<b>0.023037616</b>
20 weeks	Contral. CCR2 +/+	DMM CCR2+/+	0.29 (-0.08,0.65)	0.12453398
	Contral. CCR2 +/+	Contral. CCR2-Col1KO	0.13 (-0.27,0.53)	0.537568916
	Contral. CCR2 +/+	DMM CCR2-Col1KO	0.13 (-0.27,0.53)	0.547252234
	DMM CCR2+/+	Contral. CCR2-Col1KO	-0.16 (-0.54,0.22)	0.424023015
	DMM CCR2+/+	DMM CCR2-Col1KO	-0.16 (-0.54,0.22)	0.41560958
	Contral. CCR2-Col1KO	DMM CCR2-Col1KO	0 (-0.33,0.33)	0.987231178

**Supplemental Table S7.** Comparison between Early vs Late Recombination on PTOA parameters at 8 and 12 weeks post DMM in mouse *CCR2-Col1αKO* and *CCR2+/+* knee joint (N=8).

OA Parameters		Week 8				Week 12			
		Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)	Z (p-value)	Mean Score (Rank Sums)	median	mean (SD)
ACS	Early recombination	0.74 (0.46)	9.44	7.5	7.13(1.76)	1.05 (0.46)	9.81	7.25	6.78(3.29)
	Late Recombination		7.56	6.38	6.47(1.28)		7.19	5.5	5.53(2.51)
Saf-O	Early recombination	-1.27 (0.41)	6.94	6.63	6.42(1.62)	0.29 (0.77)	7.63	6.13	6.03(2.18)
	Late Recombination		10.06	7.5	7.44(0.75)		8.43	7	6.36(1.63)
Cartilage Histomorphometry	Early recombination	-1.1 (0.54)	7.13	18217	18364(9114)	-0.37 (0.71)	8	20436	22937(10655)
	Late Recombination		9.88	26515	24075(8390)		9	24930	25629(7527)
Osteophyte Cartilage Quantification	Early recombination	0 (1.00)	8.5	34.9	39.61(13.39)	-1.94 (0.10)	6.13	38.17	35.77(11.86)
	Late Recombination		8.5	38.43	38.27(10.71)		10.88	45.78	46.90(7.85)
Osteophyte Size	Early recombination	0.83 (0.41)	9.5	1.25	1.22(0.25)	0.92 (0.41)	9.63	1.25	1.22(0.36)
	Late Recombination		7.5	1.13	1.13(0.33)		7.38	1	1.06(0.35)
Osteophyte Maturity	Early recombination	0.5 (0.62)	9.13	1	1.06(0.32)	1.57 (0.23)	10.31	1.13	1.28(0.43)
	Late Recombination		7.88	1	0.94(0.26)		6.69	1	0.94(0.22)
%BV over TV	Early recombination	0.89 (0.37)	9.63	88.39	87.67(5.25)	-1.31 (0.37)	6.88	84.99	84.81(5.55)
	Late Recombination		7.38	85.61	85.39(4.08)		10.13	88.37	88.40(2.96)
Subchondral Bone Thickness	Early recombination	-0.68 (0.50)	7.63	159878	154086(28876)	-1.94 (0.14)	6.13	113190	118065(19106)
	Late Recombination		9.38	168541	173802(37031)		10.88	161004	152247(40161)
Synovial Hyperplasia	Early recombination	0.49 (0.62)	9.13	2	2.00(0.60)	0.71 (0.62)	9.38	2.25	2.25(0.60)
	Late Recombination		7.88	1.75	1.88(0.79)		7.63	2	2.00(0.60)

Data presented show median, mean and standard deviation (SD), for each group at separate time points (8 and 12 weeks post-surgery). Indicated z- and P-values were determined by Wilcoxon rank sum tests between DMM *CCR2+/+* and DMM *CCR2-Col1αKO* groups separately at each time point, following adjustment for multiple comparison (Benjamini-Hochberg).