

CCL24 regulates biliary inflammation and fibrosis in primary sclerosing cholangitis

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SUPPLEMENTAL MATERIAL

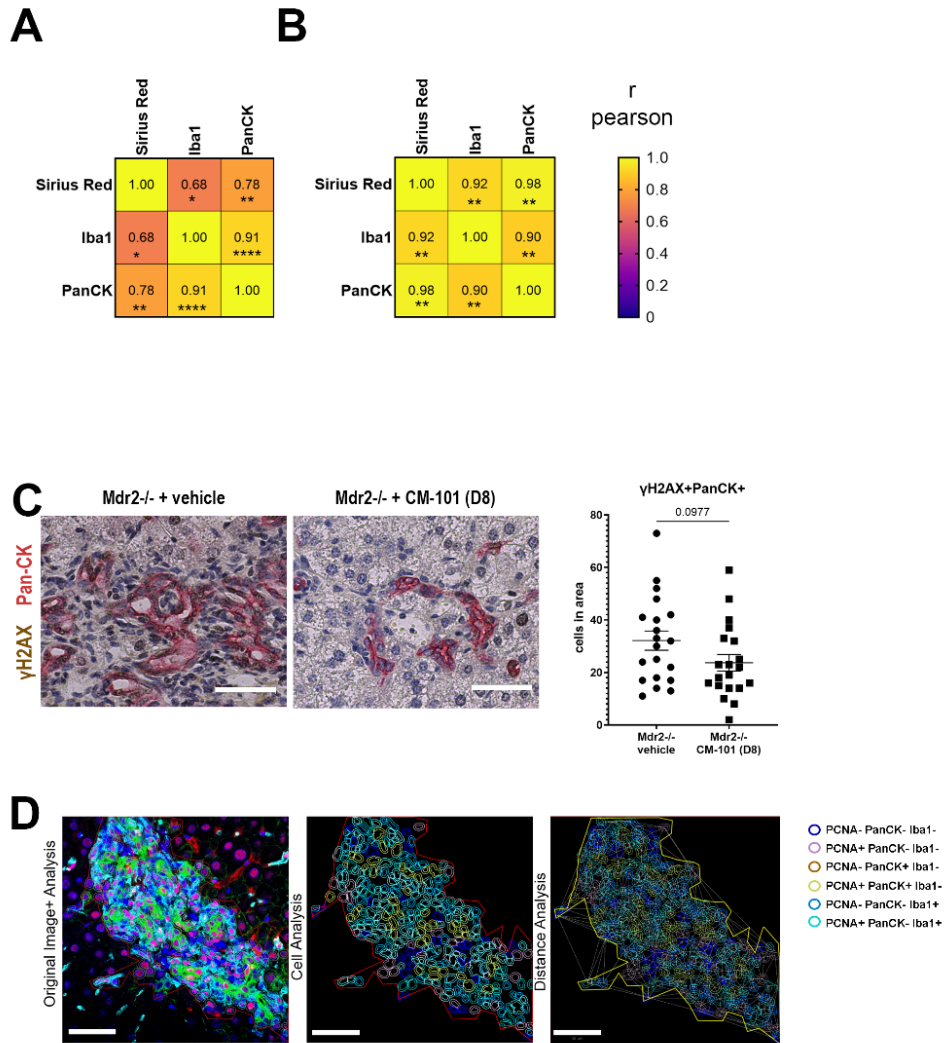


Figure S1. (A-B) Correlation matrices between Sirius Red positive stain area, Iba-1 positive stain area and Pan-CK positive stain area. Refers to figures 2 and 3. Analysis was performed on all animals (A) or on vehicle-treated animals (B). * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$. (C) Biliary senescence was measured using immunohistochemistry for Pan-CK (red) and γ H2AX (brown). Left graph shows quantification of Pan-CK⁺ γ H2AX⁺ cells per field (N = 20 fields, 4 mice per group). Data are mean \pm SEM. (D) Machine learning based cell detection Algorithm of IHC-F immunostaining in fibrotic area. Exemplary staining for Iba-1, Pan-CK, PCNA and DAPI. Left Panel: Original Image+ analysis (cell detection). Middle Panel: Analysis only (cell detection). Right Panel: Distance analysis (proximity between cells). Refers to Figures 2 and 4.

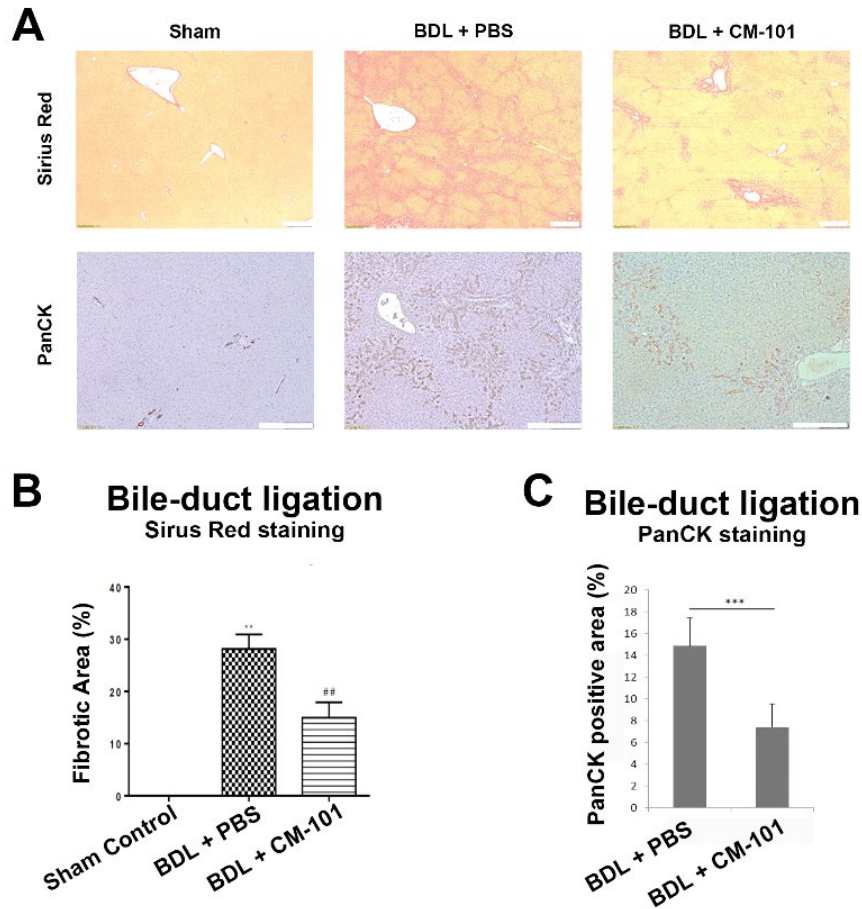


Figure S2. CM-101 treatment improves biliary damage in bile-duct ligation (BDL) rat model. (A) Representative images of Sirius Red and Pan-CK staining. Scale bar represents 200 μm . (B) Sirius Red quantitation. Results for sham control (N = 5), BDL with vehicle (N = 10) and BDL with CM-101 (N = 10) are expressed as mean + SEM. ** $p < 0.01$ vs sham control; ## $p < 0.01$ vs vehicle treated animals (BDL + PBS). Data analysis was performed by One-way ANOVA followed by Dunnett's multiple comparison test. (C) Quantification of Pan-CK staining in the liver of rats after ligation (N = 4). Data are mean \pm SEM. Data analysis was performed by One-way ANOVA followed by Dunnett's multiple comparison test. *** $p < 0.001$.

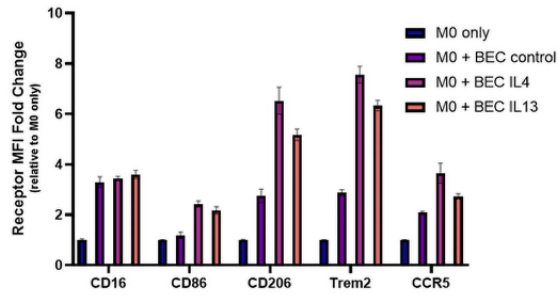
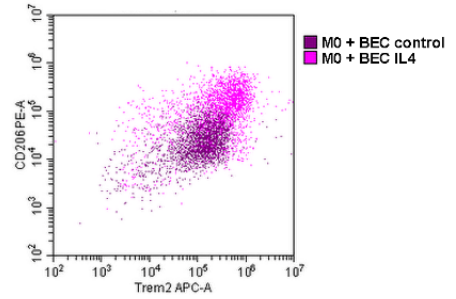
A**B**

Figure S3. Cholangiocytes induce macrophage polarization towards an M2 state.

Cholangiocytes were treated for 3 days with vehicle, IL-4 or IL-13, washed, and M0 cells were added on top of the cholangiocytes. (A) Profiling of receptor expression levels by FACS was evaluated on M0 macrophages that were grown either alone or in co-culture with pretreated BEC. Data are mean \pm SEM (N = 7). (B) Representative dot plot of CD206 and Trem2 expression in macrophages co-cultured with cholangiocytes or with cholangiocytes that had been pretreated with IL-4. Macrophages in co-culture are gated based on expression of CCR5 and CD206.

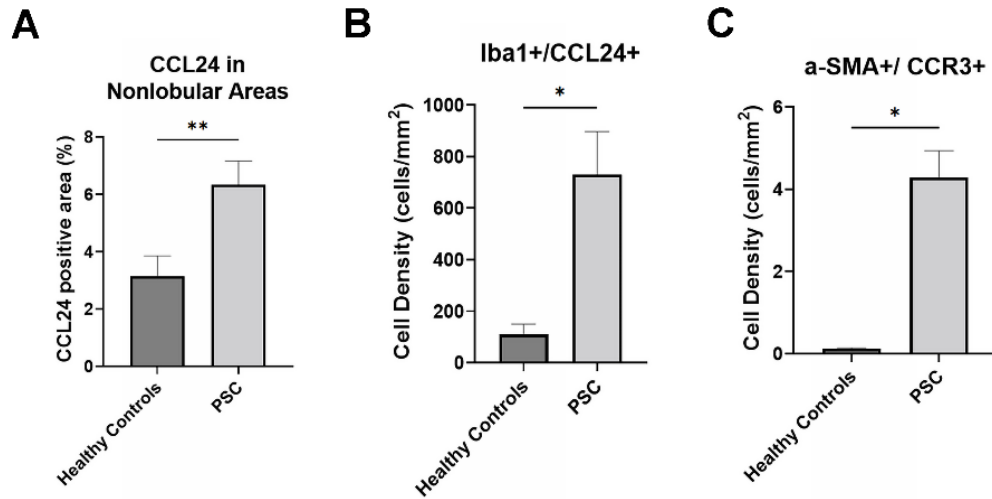


Figure S4. CCL24 and CCR3 are highly expressed in PSC patients compared to healthy controls. Refers to Figure 8. **(A)** Quantification of the area positive for CCL24 in nonlobular areas (N = 30-50 fields, 3-5 biopsies). **(B)** Quantification of cell density of Iba-1⁺/CCL24⁺ double-positive cells (N = 3-5). **(C)** Quantification of cell density of α SMA⁺/CCR3⁺ double-positive cells (N = 3-5). t-test * $p \leq 0.05$, ** $p \leq 0.01$. All results are presented as mean \pm SEM.

Table S1. Marker genes for unsupervised clustering of mononuclear phagocytes

FeatureID	Feature Name	Average	Fold Change	P-Value	Cluster	Identity
ENSMUSG00000014542	Clec4f	14.80108	4.860957	3.26E-84	1	resident macrophages
ENSMUSG00000032725	Folr2	4.191962	4.733279	5.70E-78	1	resident macrophages
ENSMUSG00000044206	Vsig4	9.871015	4.679166	6.92E-78	1	resident macrophages
ENSMUSG00000015854	Cd51	19.92701	4.5999	2.54E-75	1	resident macrophages
ENSMUSG00000055546	Timd4	2.126358	4.56854	1.98E-70	1	resident macrophages
ENSMUSG00000026390	Marco	6.048105	4.704651	1.14E-69	1	resident macrophages
ENSMUSG00000019874	Fabp7	2.350328	4.450273	2.88E-65	1	resident macrophages
ENSMUSG00000026938	Fcna	5.462336	4.324979	5.12E-64	1	resident macrophages
ENSMUSG00000022181	C6	1.932311	3.969785	5.66E-53	1	resident macrophages
ENSMUSG00000001128	Cfp	5.252874	3.777473	1.52E-49	1	resident macrophages
ENSMUSG00000069792	Wfdc17	32.41494	3.679375	1.76E-47	1	resident macrophages
ENSMUSG00000070427	Il18bp	2.24333	3.746271	2.66E-47	1	resident macrophages
ENSMUSG00000004814	Ccl24	1.178791	4.158978	1.16E-45	1	resident macrophages
ENSMUSG00000017754	Pltp	4.201937	3.487094	1.07E-41	1	resident macrophages
ENSMUSG00000023078	Cxcl13	1.57958	4.277831	2.17E-41	1	resident macrophages
ENSMUSG00000002108	Nr1h3	1.967674	3.41858	9.60E-39	1	resident macrophages
ENSMUSG00000025993	Slc40a1	4.204657	3.360957	1.89E-38	1	resident macrophages
ENSMUSG00000025743	Sdc3	4.723325	3.20343	4.47E-35	1	resident macrophages
ENSMUSG00000004730	Adgre1	3.485594	3.215013	7.61E-35	1	resident macrophages
ENSMUSG00000034641	Cd300ld	1.35833	3.182452	9.39E-33	1	resident macrophages
ENSMUSG00000034783	Cd207	1.098996	3.567659	4.56E-32	1	resident macrophages

ENSMUSG00000059089	Fcgr4	1.215968	3.090665	4.26E-30	1	resident macrophages
ENSMUSG00000030560	Ctsc	7.856189	2.919753	6.33E-29	1	resident macrophages
ENSMUSG00000024621	Csflr	6.246686	2.918532	9.73E-29	1	resident macrophages
ENSMUSG00000025498	Irf7	2.596061	2.885365	1.27E-27	1	resident macrophages
ENSMUSG00000036896	C1qc	17.88861	2.842053	4.15E-27	1	resident macrophages
ENSMUSG00000041827	Oasl1	2.550722	2.902105	8.76E-27	1	resident macrophages
ENSMUSG00000005413	Hmox1	3.072111	2.906486	6.40E-26	1	resident macrophages
ENSMUSG00000022180	Slc7a8	1.064539	2.814951	9.14E-25	1	resident macrophages
ENSMUSG00000030830	Itgal	1.904201	2.761804	1.74E-24	1	resident macrophages
ENSMUSG00000036887	C1qa	23.04809	2.652087	4.18E-23	1	resident macrophages
ENSMUSG00000046245	Pilra	1.17063	2.710032	9.17E-23	1	resident macrophages
ENSMUSG00000024397	Aifl	4.789519	2.4965	4.28E-20	1	resident macrophages
ENSMUSG00000036905	C1qb	22.20117	2.466634	1.21E-19	1	resident macrophages
ENSMUSG00000031613	Hpgd	3.18999	2.42775	5.38E-19	1	resident macrophages
ENSMUSG00000002602	Axl	2.628704	2.433103	7.35E-19	1	resident macrophages
ENSMUSG00000034708	Grn	5.46415	2.380216	1.64E-18	1	resident macrophages
ENSMUSG00000037697	Ddhd1	1.10353	2.464806	2.13E-18	1	resident macrophages
ENSMUSG00000043421	Hilpda	3.339606	2.411062	3.19E-18	1	resident macrophages
ENSMUSG00000019872	Smpd13a	2.296829	2.376739	4.46E-18	1	resident macrophages
ENSMUSG00000002699	Lcp2	1.525174	2.393275	6.15E-18	1	resident macrophages
ENSMUSG00000018217	Pmp22	1.35561	2.405083	1.19E-17	1	resident macrophages
ENSMUSG00000021939	Ctsb	24.44087	2.292551	2.80E-17	1	resident macrophages
ENSMUSG00000040713	Creg1	4.319816	2.310613	3.55E-17	1	resident macrophages
ENSMUSG00000046805	Mpeg1	4.10582	2.284735	1.21E-16	1	resident macrophages
ENSMUSG00000025746	Il6	1.380092	2.510516	1.27E-16	1	resident macrophages

ENSMUSG00000026177	Slc11a1	1.304831	2.310394	2.58E-16	1	resident macrophages
ENSMUSG00000024521	Pmaip1	1.107157	2.328804	4.25E-16	1	resident macrophages
ENSMUSG00000056091	St3gal5	1.085395	2.284992	4.38E-16	1	resident macrophages
ENSMUSG00000074622	Mafb	3.422121	2.238465	2.91E-15	1	resident macrophages
ENSMUSG00000019929	Dcn	5.441714	5.398482	5.55E-35	2	Lyve1+ resident macrophages
ENSMUSG00000026043	Col3a1	2.256523	5.317688	4.05E-28	2	Lyve1+ resident macrophages
ENSMUSG00000061353	Cxcl12	1.427653	5.172832	4.05E-28	2	Lyve1+ resident macrophages
ENSMUSG00000031375	Bgn	2.869166	4.489343	9.89E-26	2	Lyve1+ resident macrophages
ENSMUSG00000070436	Serpinh 1	1.072819	4.689727	9.89E-26	2	Lyve1+ resident macrophages
ENSMUSG00000018593	Sparc	4.216427	4.260605	1.18E-25	2	Lyve1+ resident macrophages
ENSMUSG00000026335	Pam	1.078363	4.697145	1.70E-25	2	Lyve1+ resident macrophages
ENSMUSG00000062960	Kdr	4.202566	4.201213	1.83E-25	2	Lyve1+ resident macrophages
ENSMUSG00000020044	Timp3	2.242662	4.313972	5.21E-25	2	Lyve1+ resident macrophages
ENSMUSG00000024065	Ehd3	4.654425	4.159644	6.19E-25	2	Lyve1+ resident macrophages

ENSMUSG00000058396	Gpr182	2.331371	4.227205	1.36E-24	2	Lyve1+ resident macrophages
ENSMUSG00000001506	Coll1a1	1.136578	5.066992	1.44E-24	2	Lyve1+ resident macrophages
ENSMUSG000000056492	Adgrf5	1.998714	4.200708	1.44E-24	2	Lyve1+ resident macrophages
ENSMUSG000000020154	Ptprb	5.203309	4.062582	2.68E-24	2	Lyve1+ resident macrophages
ENSMUSG000000008575	Nfib	1.521906	4.179163	9.55E-24	2	Lyve1+ resident macrophages
ENSMUSG000000030551	Nr2f2	1.197565	4.258414	1.92E-23	2	Lyve1+ resident macrophages
ENSMUSG000000004655	Aqp1	5.926838	3.987287	4.13E-23	2	Lyve1+ resident macrophages
ENSMUSG000000026678	Rgs5	1.10054	4.671473	4.29E-23	2	Lyve1+ resident macrophages
ENSMUSG000000028763	Hspg2	1.169844	4.169912	1.09E-22	2	Lyve1+ resident macrophages
ENSMUSG000000036256	Igfbp7	7.468149	3.907942	1.34E-22	2	Lyve1+ resident macrophages
ENSMUSG000000031502	Col4a1	1.435969	4.088547	1.34E-22	2	Lyve1+ resident macrophages
ENSMUSG000000058254	Tspan7	2.328599	3.976577	2.77E-22	2	Lyve1+ resident macrophages

ENSMUSG00000029648	Flt1	1.405476	4.06456	2.77E-22	2	Lyve1+ resident macrophages
ENSMUSG00000009654	Oit3	1.452602	4.071022	3.32E-22	2	Lyve1+ resident macrophages
ENSMUSG00000027210	Meis2	1.050642	4.146498	4.27E-22	2	Lyve1+ resident macrophages
ENSMUSG00000045954	Cavin2	1.313995	4.068186	6.11E-22	2	Lyve1+ resident macrophages
ENSMUSG00000031196	F8	1.355577	4.076328	7.57E-22	2	Lyve1+ resident macrophages
ENSMUSG00000074491	Clec4g	4.817982	3.860877	1.09E-21	2	Lyve1+ resident macrophages
ENSMUSG00000020357	Flt4	1.131034	4.103544	1.19E-21	2	Lyve1+ resident macrophages
ENSMUSG00000027074	Slc43a3	1.219742	4.037388	1.49E-21	2	Lyve1+ resident macrophages
ENSMUSG00000028776	Tinagl1	1.480324	3.963193	1.56E-21	2	Lyve1+ resident macrophages
ENSMUSG00000039167	Adgrl4	1.275185	4.010228	1.90E-21	2	Lyve1+ resident macrophages
ENSMUSG00000045930	Clec14a	1.247464	4.069737	2.15E-21	2	Lyve1+ resident macrophages
ENSMUSG00000026921	Egfl7	2.2787	3.879863	3.53E-21	2	Lyve1+ resident macrophages

ENSMUSG00000063415	Cyp26b 1	1.699323	3.999491	4.97E-21	2	Lyve1+ resident macrophages
ENSMUSG00000024140	Epas1	1.297362	3.921839	5.28E-21	2	Lyve1+ resident macrophages
ENSMUSG00000027800	Tm4sf1	1.671601	3.948631	5.32E-21	2	Lyve1+ resident macrophages
ENSMUSG00000054263	Lifr	2.176131	3.824845	6.21E-21	2	Lyve1+ resident macrophages
ENSMUSG00000022893	Adamts 1	1.413792	4.073055	6.74E-21	2	Lyve1+ resident macrophages
ENSMUSG00000041378	Cldn5	1.02292	4.108024	7.79E-21	2	Lyve1+ resident macrophages
ENSMUSG00000050953	Gja1	1.025692	4.063663	9.93E-21	2	Lyve1+ resident macrophages
ENSMUSG00000032766	Gng11	1.940499	3.828706	1.35E-20	2	Lyve1+ resident macrophages
ENSMUSG00000031523	Dlc1	1.413792	3.83098	1.59E-20	2	Lyve1+ resident macrophages
ENSMUSG00000054072	Iigp1	4.163756	3.707892	6.04E-20	2	Lyve1+ resident macrophages
ENSMUSG00000042284	Itga1	1.17816	3.817538	1.75E-19	2	Lyve1+ resident macrophages
ENSMUSG00000026814	Eng	3.451316	3.639443	1.90E-19	2	Lyve1+ resident macrophages

ENSMUSG00000022579	Gpihbp1	2.467206	3.71451	3.03E-19	2	Lyve1+ resident macrophages
ENSMUSG00000027358	Bmp2	3.271127	3.628961	3.60E-19	2	Lyve1+ resident macrophages
ENSMUSG00000025279	Dnase1l 3	4.86788	3.592317	7.44E-19	2	Lyve1+ resident macrophages
ENSMUSG00000021756	Il6st	2.988368	3.564082	7.73E-19	2	Lyve1+ resident macrophages
ENSMUSG00000009185	Ccl8	1.349785	5.131508	3.35E-18	3	monocyte derived macrophages
ENSMUSG00000016283	H2-M2	1.65268	3.917536	1.43E-31	3	monocyte derived macrophages
ENSMUSG00000024672	Ms4a7	4.015955	3.858461	6.25E-43	3	monocyte derived macrophages
ENSMUSG00000035352	Ccl12	1.287593	3.845169	1.65E-21	3	monocyte derived macrophages
ENSMUSG00000029373	Pf4	3.65202	3.737949	2.32E-34	3	monocyte derived macrophages
ENSMUSG00000052336	Cx3cr1	1.266863	3.60054	3.72E-33	3	monocyte derived macrophages
ENSMUSG00000069515	Lyz1	0.887956	3.059147	2.88E-09	3	monocyte derived macrophages
ENSMUSG00000023992	Trem2	1.995885	3.020582	8.73E-24	3	monocyte derived macrophages

ENSMUSG00000000982	Ccl3	10.0635	2.775273	2.78E-19	3	monocyte derived macrophages
ENSMUSG000000035373	Ccl7	6.464455	2.703376	1.42E-16	3	monocyte derived macrophages
ENSMUSG000000049130	C5ar1	1.969396	2.573783	4.78E-17	3	monocyte derived macrophages
ENSMUSG000000030144	Clec4d	1.201216	2.53169	2.38E-15	3	monocyte derived macrophages
ENSMUSG000000058755	Osm	0.673741	2.523479	1.64E-13	3	monocyte derived macrophages
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ENSMUSG000000069516	Lyz2	61.79987	2.489397	2.60E-16	3	monocyte derived macrophages
ENSMUSG000000018930	Ccl4	33.81718	2.476039	1.29E-15	3	monocyte derived macrophages
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ENSMUSG000000002985	Apoe	216.3698	2.453494	2.01E-16	3	monocyte derived macrophages
ENSMUSG000000049723	Mmp12	3.182129	2.399339	8.27E-11	3	monocyte derived macrophages
ENSMUSG000000058427	Cxcl2	66.43198	2.394532	5.27E-15	3	monocyte derived macrophages

ENSMUSG00000060586	H2-Eb1	39.06544	2.374218	7.16E-15	3	monocyte derived macrophages
ENSMUSG00000036594	H2-Aa	37.46804	2.370743	6.22E-15	3	monocyte derived macrophages
ENSMUSG00000029379	Cxcl3	1.323296	2.353299	1.10E-08	3	monocyte derived macrophages
ENSMUSG00000027995	Tlr2	1.549028	2.334115	9.57E-14	3	monocyte derived macrophages
ENSMUSG00000023913	Pla2g7	1.261104	2.330939	1.12E-13	3	monocyte derived macrophages
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ENSMUSG00000024610	Cd74	74.31878	2.317157	2.50E-14	3	monocyte derived macrophages
ENSMUSG00000038508	Gdf15	1.948665	2.252051	5.58E-11	3	monocyte derived macrophages
ENSMUSG00000043953	Ccr12	4.458205	2.214304	2.08E-12	3	monocyte derived macrophages
ENSMUSG00000052688	Rab7b	1.059558	2.214212	4.25E-12	3	monocyte derived macrophages
ENSMUSG00000073421	H2-Ab1	35.70019	2.210538	7.81E-13	3	monocyte derived macrophages
ENSMUSG00000001348	Acp5	3.820167	2.209966	1.18E-12	3	monocyte derived macrophages

ENSMUSG00000059498	Fcgr3	1.641163	2.193414	2.93E-12	3	monocyte derived macrophages
ENSMUSG00000023349	Clec4n	1.957879	2.17395	7.79E-12	3	monocyte derived macrophages
ENSMUSG00000079547	H2- DMb1	2.409343	2.128209	1.19E-11	3	monocyte derived macrophages
ENSMUSG00000112023	Lilr4b	1.50296	2.127578	1.47E-11	3	monocyte derived macrophages
ENSMUSG00000026981	Il1rn	3.660082	2.123362	2.15E-11	3	monocyte derived macrophages
ENSMUSG00000036905	C1qb	20.58998	2.121785	6.67E-12	3	monocyte derived macrophages
ENSMUSG00000056529	Ptafr	1.555938	2.097433	3.33E-11	3	monocyte derived macrophages
ENSMUSG00000038642	Ctss	11.21519	2.077716	1.81E-11	3	monocyte derived macrophages
ENSMUSG00000036887	C1qa	19.25171	2.048065	5.24E-11	3	monocyte derived macrophages
ENSMUSG00000089929	Bcl2a1b	6.282488	2.001983	1.74E-10	3	monocyte derived macrophages
ENSMUSG00000029380	Cxcl1	9.328717	1.975358	9.70E-10	3	monocyte derived macrophages
ENSMUSG00000019122	Ccl9	2.43468	1.950773	3.37E-09	3	monocyte derived macrophages

ENSMUSG00000072620	Slfn2	4.018258	1.943894	7.48E-10	3	monocyte derived macrophages
ENSMUSG00000044811	Cd300c 2	2.466927	1.928809	1.18E-09	3	monocyte derived macrophages
ENSMUSG00000024401	Tnf	4.420199	1.924498	3.43E-09	3	monocyte derived macrophages
ENSMUSG00000015396	Cd83	5.46133	1.916653	1.41E-09	3	monocyte derived macrophages
ENSMUSG00000027399	Il1a	5.915098	1.914371	1.51E-09	3	monocyte derived macrophages
ENSMUSG00000036896	C1qc	13.06366	1.909386	1.68E-09	3	monocyte derived macrophages
ENSMUSG00000040809	Chil3	2.028774	5.383906	1.11E-28	4	tissue monocytes
ENSMUSG00000029378	Areg	1.739482	4.098982	1.96E-19	4	tissue monocytes
ENSMUSG00000041324	Inhba	1.453923	4.019549	1.12E-24	4	tissue monocytes
ENSMUSG00000022018	Rgcc	1.231822	3.650665	3.94E-22	4	tissue monocytes
ENSMUSG00000029379	Cxcl3	2.683879	3.649627	1.40E-16	4	tissue monocytes
ENSMUSG00000033213	AA4671 97	3.361381	3.632307	1.69E-21	4	tissue monocytes
ENSMUSG00000058755	Osm	1.198227	3.50303	8.92E-21	4	tissue monocytes
ENSMUSG00000069515	Lyz1	1.243021	3.43422	1.35E-08	4	tissue monocytes
ENSMUSG00000030142	Clec4e	3.943697	3.375328	4.12E-20	4	tissue monocytes
ENSMUSG00000019122	Ccl9	4.949686	3.196459	1.17E-19	4	tissue monocytes
ENSMUSG00000027737	Slc7a11	1.498717	3.127887	2.00E-16	4	tissue monocytes
ENSMUSG00000017002	Slpi	1.834669	3.073825	5.29E-10	4	tissue monocytes

ENSMUSG00000049723	Mmp12	4.87503	3.028107	1.35E-12	4	tissue monocytes
ENSMUSG00000050335	Lgals3	14.46458	3.015229	1.37E-17	4	tissue monocytes
ENSMUSG00000049103	Ccr2	1.338207	2.972832	1.87E-15	4	tissue monocytes
ENSMUSG00000032487	Ptgs2	3.887705	2.940588	7.21E-15	4	tissue monocytes
ENSMUSG00000030789	Itgax	1.149701	2.930063	1.49E-15	4	tissue monocytes
ENSMUSG00000031444	F10	1.403531	2.910609	5.85E-15	4	tissue monocytes
ENSMUSG00000001020	S100a4	6.116184	2.887369	5.44E-14	4	tissue monocytes
ENSMUSG00000030144	Clec4d	1.584571	2.829408	2.14E-14	4	tissue monocytes
ENSMUSG00000040152	Thbs1	5.832491	2.808984	2.34E-13	4	tissue monocytes
ENSMUSG00000069516	Lyz2	80.29614	2.759482	2.00E-14	4	tissue monocytes
ENSMUSG00000056737	Capg	2.286337	2.639757	1.22E-12	4	tissue monocytes
ENSMUSG00000024659	Anxa1	1.653628	2.55727	8.67E-12	4	tissue monocytes
ENSMUSG00000027995	Tlr2	1.939187	2.546221	1.84E-11	4	tissue monocytes
ENSMUSG00000029322	Plac8	4.738783	2.531676	9.06E-11	4	tissue monocytes
ENSMUSG00000023349	Clec4n	2.562563	2.489782	6.89E-11	4	tissue monocytes
ENSMUSG00000038352	Arl5c	1.40913	2.440959	1.81E-10	4	tissue monocytes
ENSMUSG00000027398	Il1b	38.98717	2.407755	1.49E-10	4	tissue monocytes
ENSMUSG00000079293	Clec7a	5.186718	2.38309	3.49E-10	4	tissue monocytes
ENSMUSG00000035678	Tnfsf9	1.149701	2.362532	1.59E-09	4	tissue monocytes
ENSMUSG00000018927	Ccl6	4.6156	2.299958	3.16E-09	4	tissue monocytes
ENSMUSG00000046223	Plaur	3.260596	2.281232	2.77E-09	4	tissue monocytes
ENSMUSG00000051439	Cd14	12.34435	2.256193	4.11E-09	4	tissue monocytes
ENSMUSG00000026981	Il1rn	4.244187	2.211925	1.93E-08	4	tissue monocytes
ENSMUSG00000000290	Itgb2	1.640563	2.203333	7.40E-09	4	tissue monocytes
ENSMUSG00000060063	Alox5ap	2.03064	2.192362	2.78E-08	4	tissue monocytes

ENSMUSG00000058427	Cxcl2	66.89168	2.178394	2.31E-08	4	tissue monocytes
ENSMUSG00000030707	Coro1a	2.784665	2.17776	2.64E-08	4	tissue monocytes
ENSMUSG00000026193	Fn1	2.730539	2.15514	1.04E-07	4	tissue monocytes
ENSMUSG00000043953	Ccr12	4.645463	2.091793	1.88E-07	4	tissue monocytes
ENSMUSG00000079419	Ms4a6c	2.092231	2.083584	1.68E-07	4	tissue monocytes
ENSMUSG00000056529	Ptafr	1.702154	2.081526	1.87E-07	4	tissue monocytes
ENSMUSG00000016283	H2-M2	0.920134	2.073291	1.90E-05	4	tissue monocytes
ENSMUSG00000035493	Tgfbi	2.265806	2.06463	4.38E-07	4	tissue monocytes
ENSMUSG00000041836	Ptpre	1.06198	2.051784	1.52E-07	4	tissue monocytes
ENSMUSG00000002204	Napsa	0.963061	2.04713	1.20E-06	4	tissue monocytes
ENSMUSG00000072620	Slfn2	4.626799	2.039828	2.28E-07	4	tissue monocytes
ENSMUSG00000024401	Tnf	5.098997	2.025864	6.48E-07	4	tissue monocytes
ENSMUSG00000022126	Acod1	1.646162	2.022958	1.44E-06	4	tissue monocytes
ENSMUSG00000076613	Ighg2b	2.330353	11.6269	0.000771	5	dendritic cells
ENSMUSG00000031494	Cd209a	1.070824	6.160389	3.30E-60	5	dendritic cells
ENSMUSG00000004296	Il12b	1.485675	5.869473	1.66E-29	5	dendritic cells
ENSMUSG00000031780	Ccl17	5.1759	5.85284	2.03E-50	5	dendritic cells
ENSMUSG00000037548	H2- DMb2	1.22059	5.41555	4.04E-63	5	dendritic cells
ENSMUSG00000037944	Ccr7	3.522487	5.243447	1.88E-57	5	dendritic cells
ENSMUSG00000031779	Ccl22	4.07662	5.196518	8.24E-49	5	dendritic cells
ENSMUSG00000002204	Napsa	2.301897	4.366014	2.55E-47	5	dendritic cells
ENSMUSG00000029413	Naaa	1.758248	4.18737	5.82E-42	5	dendritic cells
ENSMUSG00000051506	Wdfy4	1.235566	4.139961	7.44E-43	5	dendritic cells
ENSMUSG00000018819	Lsp1	4.185949	4.010017	1.78E-42	5	dendritic cells

ENSMUSG00000033083	Tbc1d4	2.099714	3.857039	2.06E-34	5	dendritic cells
ENSMUSG00000027447	Cst3	77.28804	3.554179	5.86E-33	5	dendritic cells
ENSMUSG00000040950	Mgl2	1.030387	3.406314	2.54E-20	5	dendritic cells
ENSMUSG00000001020	S100a4	6.755927	3.295393	9.35E-24	5	dendritic cells
ENSMUSG00000026073	Il1r2	1.021401	3.274859	1.59E-20	5	dendritic cells
ENSMUSG00000028341	Nr4a3	3.279867	3.220365	7.17E-24	5	dendritic cells
ENSMUSG00000026832	Cytip	3.477558	3.190101	1.63E-24	5	dendritic cells
ENSMUSG00000040710	St8sia4	1.298468	3.141246	2.21E-22	5	dendritic cells
ENSMUSG00000030214	Plbd1	2.942894	3.083812	1.08E-22	5	dendritic cells
ENSMUSG00000085156	Snhg15	1.075317	3.083138	4.87E-21	5	dendritic cells
ENSMUSG00000019876	Pkib	1.189139	3.013303	7.64E-21	5	dendritic cells
ENSMUSG00000000531	Grasp	1.377844	3.001097	1.70E-20	5	dendritic cells
ENSMUSG00000034634	Ly6d	1.494661	2.916121	1.21E-09	5	dendritic cells
ENSMUSG00000018821	Avp1l	1.13073	2.672699	9.37E-16	5	dendritic cells
ENSMUSG00000070691	Runx3	1.027392	2.653182	7.38E-15	5	dendritic cells
ENSMUSG00000026875	Traf1	2.129667	2.642199	4.83E-15	5	dendritic cells
ENSMUSG00000000594	Gm2a	4.31924	2.613324	1.26E-15	5	dendritic cells
ENSMUSG00000076609	Igkc	8.403349	2.540991	0.041208	5	dendritic cells
ENSMUSG00000073421	H2-Ab1	44.52681	2.535194	1.51E-14	5	dendritic cells
ENSMUSG00000060063	Alox5ap	2.25547	2.495003	1.85E-13	5	dendritic cells
ENSMUSG00000033213	AA4671 97	1.908014	2.488443	3.22E-10	5	dendritic cells
ENSMUSG00000028657	Ppt1	1.470698	2.455601	6.14E-13	5	dendritic cells
ENSMUSG00000030707	Coro1a	3.037247	2.440628	5.10E-13	5	dendritic cells
ENSMUSG00000001270	Ckb	3.128604	2.437539	4.59E-13	5	dendritic cells

ENSMUSG00000060586	H2-Eb1	42.2983	2.393606	1.23E-12	5	dendritic cells
ENSMUSG00000095079	Igha	1.308951	2.379745	0.195458	5	dendritic cells
ENSMUSG00000048163	Selplg	1.286487	2.371085	4.84E-12	5	dendritic cells
ENSMUSG00000048277	Syngn2	2.149137	2.330279	7.34E-12	5	dendritic cells
ENSMUSG00000037649	H2- DMa	3.413158	2.296817	1.90E-11	5	dendritic cells
ENSMUSG00000003382	Etv3	1.68037	2.246597	1.11E-10	5	dendritic cells
ENSMUSG00000022205	Sub1	5.054589	2.245928	3.82E-11	5	dendritic cells
ENSMUSG00000022876	Samsn1	1.289482	2.240562	3.09E-10	5	dendritic cells
ENSMUSG00000036594	H2-Aa	37.55223	2.233542	8.38E-11	5	dendritic cells
ENSMUSG00000006360	Crip1	13.01463	2.200013	2.51E-10	5	dendritic cells
ENSMUSG00000037894	H2az1	12.3332	2.151386	3.33E-10	5	dendritic cells
ENSMUSG00000026826	Nr4a2	1.476689	2.13373	4.15E-09	5	dendritic cells
ENSMUSG00000024610	Cd74	72.24693	2.125871	1.02E-09	5	dendritic cells
ENSMUSG00000067149	Jchain	0.569109	2.06072	0.116278	5	dendritic cells
ENSMUSG00000000682	Cd52	13.27073	2.049297	4.74E-09	5	dendritic cells

Table S2. Clinical characteristics of patients in serum analysis

N	20
Men, n (%)	10 (50%)
Age, yr, median (IQR)	49.5 (31.5-64)
IBD any, n (%)	7 (35%)
Hepatobiliary malignancies any, n (%)	0 (0%)
Fibrosis stage, median (range)	F3 (F1-F3)
ELF, median (IQR)	10 (9.2-10.9)
ALP, median (IQR)	265 (172-453)
Bilirubin, median (IQR)	12 (6.3-17)
AST, median (IQR)	48 (34.8-76)
ALT, median (IQR)	63.5 (46-148)
Creatinine, median (IQR)	69 (57.3-77)
PLT, median (IQR)	268 (223-360)
WCC, median (IQR)	7.2 (5.2-7.6)
INR, median (IQR)	1 (1-1.1)

Table S3. ANOVA followed by Holm-Šídák's multiple comparisons test Statistical Analysis

ANOVA summary	F	P value	P value summary
ALT	9.849	<0.0001	****
ALP	7.199	0.0003	***
BA	6.624	0.0007	***
Col1A1	4.668	0.0133	*
Timp1	4.318	0.018	*
LX2 CCL24 RNA	45.25	<0.0001	****
BEC CCL24 RNA	40.68	<0.0001	****
BEC CCL24 ELISA	111.1	<0.0001	****
HSC proliferation by CFSE	15.47	0.0005	***
HSC proliferation by cell number	25.78	<0.0001	****
LX2 proliferation	19.43	<0.0001	****
BEC proliferation by CFSE: Co-culture	1.58	0.2197	ns
BEC proliferation by CFSE: CM-101 treatment	36.11	<0.0001	****
BEC proliferation by CFSE: Interaction	4.12	0.0171	*
BEC proliferation by Ki67: Co-culture	24.68	0.0998	ns
BEC proliferation by Ki67: CM-101 treatment	96.96	<0.0001	****
BEC proliferation by Ki67: Interaction	2.33	<0.0001	****
	Mean	Adjusted	P value
Holm-Šídák's multiple comparisons test	Diff.	P Value	Summary
<u>ALT</u>			
Mdr2 ^{-/-} vs. WT	160.9	<0.0001	****

Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 5mg/kg	24.75	0.3001	ns
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 10mg/kg	58.35	0.0247	*
<u>ALP</u>			
Mdr2 ^{-/-} vs. WT	38.51	0.0026	**
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 5mg/kg	17.65	0.0505	ns
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 10mg/kg	33.61	0.0006	***
<u>BA</u>			
Mdr2 ^{-/-} vs. WT	24.96	0.0012	**
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 5mg/kg	13.74	0.0081	**
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 10mg/kg	10.2	0.0263	*
<u>Col1A1</u>			
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 5mg/kg	0.1444	0.2756	ns
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 10mg/kg	0.4091	0.0069	**
<u>Timp1</u>			
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 5mg/kg	-0.02826	0.8737	ns
Mdr2 ^{-/-} vs. Mdr2 ^{-/-} 10mg/kg	0.4851	0.019	*
<u>BEC CCL24 RNA</u>			
control vs. IL-4	-13.97	<0.0001	****
control vs. IL-13	-11.78	<0.0001	****
<u>BEC CCL24 ELISA</u>			
control vs. IL-4	-11.64	<0.0001	****

control vs. IL-13	-11.27	<0.0001	****
control vs. TGF-b	1.13	0.37	ns
control vs. LPS	-0.08633	0.9203	ns
control vs. TNF-a	1.67	0.2	ns
<u>LX2 proliferation</u>			
Control vs. CCL24 25ng/ml	-0.1574	0.0047	**
Control vs. CCL24 25ng/ml+ CM-101 1ug/ml	-0.03845	0.8394	ns
Control vs. CCL24 25ng/ml+ CM-101 2.5ug/ml	-0.0021	0.95	ns
Control vs. CCL24 50ng/m	-0.2548	<0.0001	****
Control vs. CCL24 50ng/ml+ CM-101 1ug/ml	-0.1344	0.0146	*
Control vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.01791	0.9357	ns
CCL24 25ng/ml vs. CCL24 25ng/ml+ CM-101 1ug/ml	0.1189	0.0282	*
CCL24 25ng/ml vs. CCL24 25ng/ml+ CM-101 2.5ug/ml	0.1553	0.005	**
CCL24 25ng/ml vs. CCL24 50ng/m	-0.09744	0.0897	ns
CCL24 25ng/ml vs. CCL24 50ng/ml+ CM-101 1ug/ml	0.02301	0.9357	ns
CCL24 25ng/ml vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.1753	0.0018	**
CCL24 25ng/ml+ CM-101 1ug/ml vs. CCL24 25ng/ml+ CM-101 2.5ug/ml	0.03635	0.8394	ns
CCL24 25ng/ml+ CM-101 1ug/ml vs. CCL24 50ng/m	-0.2164	0.0002	***
CCL24 25ng/ml+ CM-101 1ug/ml vs. CCL24 50ng/ml+ CM-101 1ug/ml	-0.09591	0.0897	ns
CCL24 25ng/ml+ CM-101 1ug/ml vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.05636	0.555	ns
CCL24 25ng/ml+ CM-101 2.5ug/ml vs. CCL24 50ng/m	-0.2527	<0.0001	****
CCL24 25ng/ml+ CM-101 2.5ug/ml vs. CCL24 50ng/ml+ CM-101 1ug/ml	-0.1323	0.0153	*
CCL24 25ng/ml+ CM-101 2.5ug/ml vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.02001	0.9357	ns
CCL24 50ng/m vs. CCL24 50ng/ml+ CM-101 1ug/ml	0.1205	0.0282	*
CCL24 50ng/m vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.2727	<0.0001	****

CCL24 50ng/ml+ CM-101 1ug/ml vs. CCL24 50ng/ml+ CM-101 2.5ug/ml	0.1523	0.0055	**
<u>HSC proliferation by CFSE</u>			
control vs. CCL24	-0.1594	0.0007	***
control vs. CCL24+CM-101	-0.01032	0.7888	ns
CCL24 vs. CCL24+CM-101	0.149	0.0038	**
<u>HSC proliferation by cell number</u>			
control vs. CCL24	-0.5172	<0.0001	****
CCL24 vs. CCL24+CM-101	0.4792	0.0003	***
<u>LX2 CCL24 RNA</u>			
control vs. IL4	-5.477	<0.0001	****
control vs. M0-CM	-0.02823	0.9680	ns
control vs. M0-CM + IL4	-3.858	0.0013	**
control vs. M2-CM	-7.892	<0.0001	****
IL4 vs. M0-CM	5.448	<0.0001	****
IL4 vs. M0-CM + IL4	1.619	0.1220	ns
IL4 vs. M2-CM	-2.415	0.0285	*
M0-CM vs. M0-CM + IL4	-3.830	0.0006	***
M0-CM vs. M2-CM	-7.864	<0.0001	****
M0-CM + IL4 vs. M2-CM	-4.034	0.0011	**