

## Supplementary Materials

### Genetic influence on frequencies of myeloid-derived cell subpopulations in mouse

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**Supplementary Table 1. List of antibodies used for immunophenotyping**

Antibody	Clone	Catalog number	Company
fluorescein isocyanate (FITC)-labeled anti-CD4	GK1.5	100406	BioLegend, San Diego, CA
phycoerythrin (PE)-labeled anti-CD8	53-6.7	100708	BioLegend, San Diego, CA
allophycocyanine (APC)-labeled anti-CD3	17A2	100236	BioLegend, San Diego, CA
APC anti-mouse/human CD11b	M1/70	101212	BioLegend, San Diego, CA
PE anti-mouse F4/80	BM8	123110	BioLegend, San Diego, CA
PE anti-mouse CD14	Sa14-2	123310	BioLegend, San Diego, CA
FITC anti-mouse CD19	6D5	115506	BioLegend, San Diego, CA
FITC anti-mouse Ly-6G/Ly-6C (Gr1)	RB6-8C5	108406	BioLegend, San Diego, CA
Alexa Fluor 647 anti-mouse CD22	OX-97	126108	BioLegend, San Diego, CA
FITC anti-mouse CD40	HM40-3	09404D	BD Pharmingen
PE anti-mouse Siglec-F	E50-2440	562068	BD Pharmingen
PE anti-mouse CD86	B7-2	553692	BD Pharmingen
Pacific Blue anti-TER119	TER119	116208	BioLegend, San Diego, CA

**Supplementary Table 2. List of primers used for RT PCR experiments**

<b>Gene of interest</b>	<b>Forward primer</b>	<b>Reverse primer</b>
<i>Smad1</i>	TGGACACCAGAACAGATACAGTGC	CTGTGGTCTTCGAAAGTTCTCTGG
<i>Mir30a</i>	GCGACTGTAAACATCCTCGAC	CAGCTGCAAACATCCGACTG
<i>Mir30c-2</i>	TGTAAACATCCTACACTCTCAGC	AGGCAGAGAGAGTAAACAGCC
<i>Ogfr11</i>	CAGTCGGCTTTGCTGTATTGCC	TGCCAGTTTCATCTCTGGCAGTC
<i>Col9a1</i>	TGAGACCCAGGAGAGAAACCTGTC	TCATCAGTGGTCTGGCTGGTTG
<i>Foxred2</i>	AGATGTTCAGTGTGCTGGCTGAC	ACTCAAAGGCTGTGGCGTTCTC
<i>Trem12</i>	CGGCTGGGCATTTCTACCCT	TCCATCCATGGGGGTGTTGG
<i>Vps52</i>	CGCTGAGCAAGATCTACCTGTC	CTCAGCAACTTCCTCGTACTGC
<i>Lst1</i>	TTGTGCCGGTTCAGTCAGAGAGTG	GGCATAGTCAGTGCTGAGGTCTTC
<i>TnxB</i>	TTGGACTCAAGGATGGGAAGCG	AGCAGCTTTGCATCAGAGACAG
<i>Pla2g7</i>	ATCCTCGTGTGCAGATCTGTGG	ACATGGCCCTTTCTGCCTGTTC
<i>Rab44</i>	GGCAGATAGAGGAAGAGCCAAGTG	AATGGGCTTCAATGCTGCTGAGG
<i>Olf113</i>	TGCTCAAGTTCTCCTGCTCTGATG	AGACAGGAAATCAGCCACTCCAAC
<i>Ephx3</i>	CAGGGTGAGTGTTCCTCCCG	ACGCATGTCTACAGCCACGA
<i>H2-M5</i>	GTTTACTGGAGCTGTGGTTGCC	CAGAATTCCTGGGTTTCAGCCCT
<i>Ptx4</i>	TCACCCAGCCAGGCAAAGAA	GGCTCTGGAAGCGAACATCC
<i>Gm4841</i>	TCTGTGCATCCTGCTCTGAGTG	GGTGTGTGTGTGTGTGTGTGTG
<i>F830016B08Rik</i>	TTACGGAGGCAGCCACTGAAAG	GGCTTCTAGCCAGATAAACTGCTG
<i>Alpk2</i>	TGCTTCGATGCATGATAGCTGGTC	TGGAAACAGTGCCTCCCAAGTC
<i>Megf10</i>	TGTGACTGCTTACCTGGCTTCAC	ATCTGCCACTGGGACACACTTC
<i>GAPDH</i>	AACTTTGGCATTGTGGAAGG	GTCTTCTGGGTGGCAGTGAT

**Supplementary Table 3. Functions of genes localized in *Mydc1***

<b>Gene (Name)</b>	<b>Function</b>
<i>4933415F23Rik=Ppp1r14bl</i> (phosphatase 1, regulatory inhibitor subunit 14B like)	Protein serine/threonine phosphatase inhibitor activity (1).
<i>Mir30a</i> (microRNA 30a)	Alters the expression of myeloid differentiation primary response 88 (2), controls the instability of inducible CD4+ Tregs through SOCS1 (3) and reduces the suppressive function of iTregs (3), inhibits of differentiation of Th17 (4).
<i>Mir30c-2</i> (microRNA 30c-2)	Regulates proliferation, apoptosis and differentiation via the Shh signaling pathway (5), regulates macrophage-mediated inflammation (6), and is involved in Th17 differentiation (7).
<i>Ogfr1l</i> (opioid growth factor receptor-like 1)	A bone-marrow cell-derived accelerator of fibrotic liver regeneration in response to G-CSF treatment. Stimulates proliferation of hepatic parenchymal cell (8).
<i>B3gat2</i> (beta-1,3-glucuronyltransferase 2 = glucuronosyltransferase S)	Catalyzes the transfer of a beta-1,3 linked glucuronic acid to a terminal galactose in different glycoproteins or glycolipids (9).
<i>Smap1</i> (small ArfGAP1 = small ADP-ribosylation factor GTPase-activating protein 1)	An ARF6 GTPase-activating protein that functions in clathrin-dependent endocytosis and plays role in blood cell proliferation and development (10). ARF6 participates in functions of polymorphonuclear leukocytes (11).
<i>Sdhaf4 = Sdh8</i> (succinate dehydrogenase complex assembly factor 4)	<i>Sdhaf4</i> interacts specifically with the catalytic Sdh1 subunit in the mitochondrial matrix, facilitating its association with Sdh2 and the subsequent assembly of the SDH (succinate dehydrogenase) holocomplex. It prevents neurodegeneration (12).
<i>Col9a1</i> (collagen, type IX, alpha 1)	A heterotrimer of 1(IX), 2(IX), and 3(IX) polypeptide chains that fold into the triple helix c; only alpha 1 chain forms NC4 domain participates in electrostatic interactions with polyanionic glycosaminoglycans in cartilage (13), the loss of <i>Col9a1</i> destabilizes the trabecular bone network, and impairs myeloid cell differentiation in bone marrow (14).

**Supplementary Table 4. Expression of genes in *Mydc1* in organs of uninfected mice**

Gene symbol	<i>4933415f23rik</i>	<i>mir30a</i>	<i>mir30c-2</i>	<i>Ogfr1</i>	<i>Smap1</i>	<i>Sdhaf4</i>	<i>Col9a1</i>	<i>B3gat2</i>
gene ID: MGI	1914005	2676907	3619048	1917405	2138261	1915252	88465	2389490
gene ID: NCBI	66755	387225	723964	70155	98366	68002	12839	280645
median	4.6	N/A	N/A	33.7	80.5	482	5.3	4.6
<b>Organs</b>								
Spleen	4.6 =M	N/A	N/A	40.83 >M	84.82 >M	340 <M	4.87 <M	4.64 ~M
Bone marrow	4.6 =M	N/A	N/A	203 >3M	366 >3M	323 <M	5.11 ~M	4.8 ~M
Lymph nodes	4.6 =M	N/A	N/A	67.02 >M	57.3 <M	352 <M	4.69 <M	4.64 ~M
Liver	4.6 =M	N/A	N/A	55.15 >M	81.34 ~M	749 >M	4.87 <M	4.64 ~M
<b>Organ with highest expression</b>	testis >30M	N/A	N/A	mammary gland >30M	testis >10M	heart >3M	mammary gland >30M	kidney >3M
<b>Expression in other organs</b>				dorsal root ganglia >10M				

**Abbreviations:** N/A: Not assessed. In **bold**: three fold or higher expression. Data were compiled from public database BioGPS (<http://biogps.org>) November 3, 2021. First column: relative units; Second column: relationship to median (M); M=median value across all samples for a single probe set. Color scale: blue: lower than median, gray: similar to median, yellow to dark orange: higher than median (the intensity of yellow color is relative to the expression level as indicated)

**Supplementary Table 5: Expression status of undetected genes (*Ptx4*, *Ephx3*, *H2-Q1*, *H2-M5*, *F830016B08Rik*, *Megf10*) in spleen of healthy mice of strains DBA/2JxC57BL/6J; CD1; C57BL/6J and DBA. Data was compiled from GXD (15) and Expression Atlas (16), Dec 12, 2020.**

	<i>Ptx4</i>	<i>Ephx3</i>	<i>H2-Q1</i>	<i>H2-M5</i>	<i>F830016B08Rik</i>	<i>Megf10</i>	<i>Reference</i>
Summary of expression	no	yes - low	yes - low	yes - low	yes - low	Very low	
DBA/2J x C57BL/6J	no	yes - low	yes - low	yes - low	yes - low	yes - low	17
CD1	no	yes - low	yes - low	yes - low	yes - low	no - below cut-off	18
C57BL6/J	no	yes - low	no	yes - low	yes - low	No	18
DBA	no	yes - low	yes - low	yes - low	yes - low	no	18

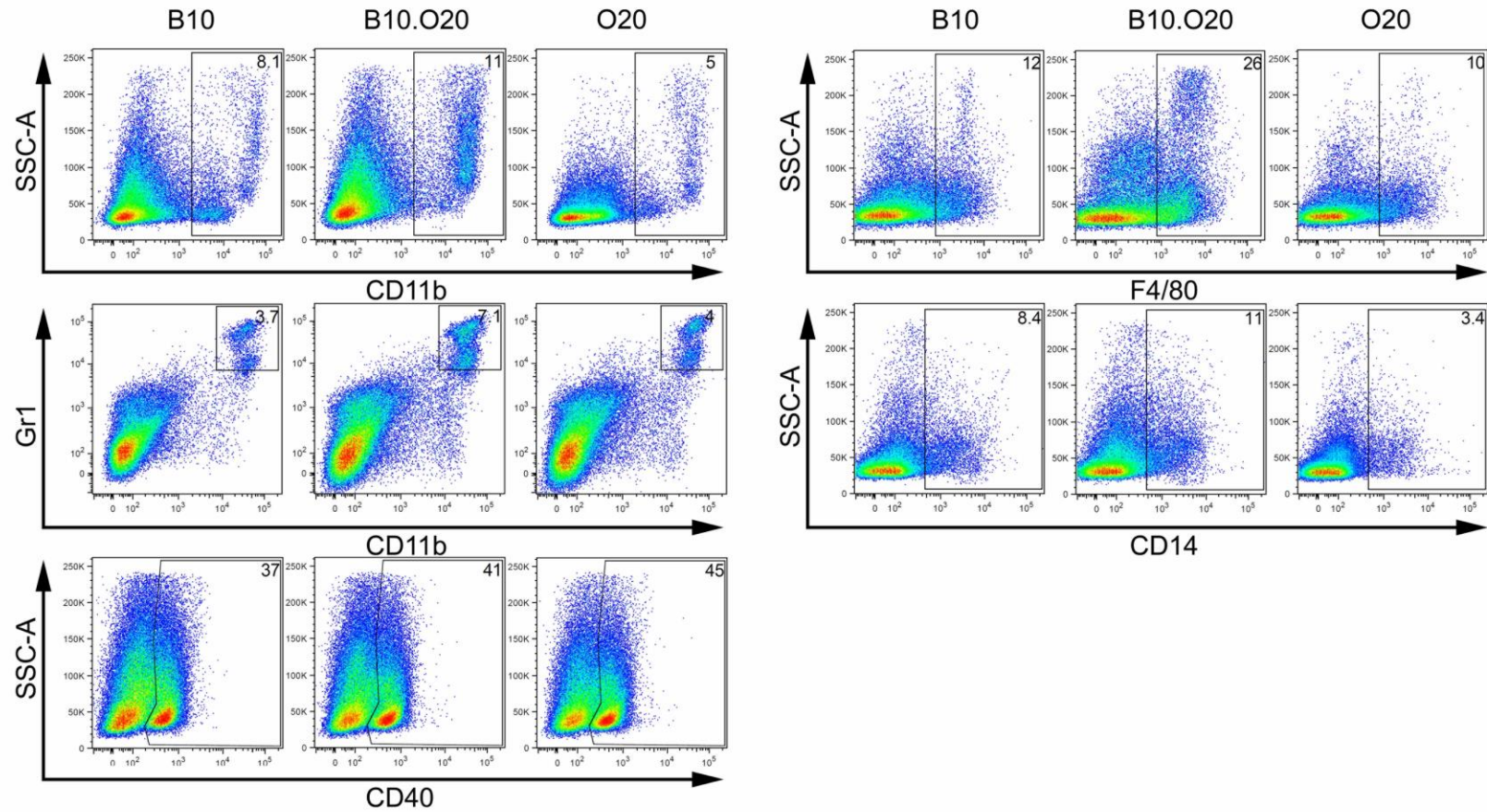
**Supplementary Table 6. Expression of potential candidate genes in organs and cells of uninfected mice**

Gene symbol	<i>Foxred2</i>	<i>Gtpbp1</i>	<i>Rab44</i>	<i>Cyp4f13</i>	<i>4921501E</i> <i>09Rik</i> ( <i>Phf8-ps</i> )	<i>Vps52</i>	<i>H2-Eb2</i>	<i>Tnxb</i>	<i>Gpr115</i>	<i>Pla2g7</i>	<i>Mymx</i>	<i>AI661453</i>	<i>Zfp52</i>
Chromosome	15	15	17	17	17	17	17	17	17	17	17	17	17
gene ID: MGI	106315	109443	3045302	2158641	1921292	1330304	95902	1932137	1925499	1351327	3649059	2146908	99199
Gene ID: NCBI	239554	14904	442827	170716	74042	224705	381091	81877	78249	27226	653016	224833	22710
Median	62.7	103.0	4.6	21.8	4.6	26.7	11.8	4.6	4.6	132.9	4.9	9.0	14.4
<b>Organs</b>													
Bone marrow	68.3 >M	322.3 >3M	345.2 >30M	11.7 <M	4.6 ~M	144.3 >3M	13.6 >M	4.6 <M	4.6 ~M	483.6 >3M	4.6 <M	8.3 <M	11.1 <M
Liver	5.8 <M	79.4 <M	4.6 ~M	533.1 >10M	4.6 ~M	42.2 >M	11.7 <M	19.1 >3M	4.6 ~M	35.9 <M	4.6 <M	116.8 >10M	5.7 <M
Lymph nodes	44.4 <M	250.3 >M	4.6 ~M	30.1 >M	4.6 ~M	111.7 >3M	381.3 >30M	23.3 >3M	4.6 ~M	1179.9 >3M	4.6 <M	8.1 <M	33.3 >M
Spleen	63.9 >M	233.4 >M	5.9 >M	14.1 <M	5.4 ~M	88.3 >3M	239.0 >10M	377.4 >30M	4.6 ~M	846.9 >3M	4.6 <M	8.3 <M	71.3 >3M
<b>Cells</b>													
B-cells MZ	114.7 >M	52.3 <M	4.6 ~M	51.2 >M	4.6 ~M	176.1 >3M	530.9 >30M	4.6 ~M	4.6 ~M	108.9 <M	5.1 >M	9.0 ~M	254.6 >10M
CMP	342.2 >3M	218.3 >M	181.6 >30M	21.3 <M	4.6 ~M	161.6 >3M	15.0 >M	4.6 ~M	4.6 ~M	4.8 <M	4.6 <M	13.4 >M	63.5 >3M
DCL CD8a+	49.5 <M	173.9 >M	4.6 ~M	18.5 <M	4.6 ~M	144.7 >3M	198.6 >10M	4.6 ~M	4.6 ~M	27.2 <M	4.9 ~M	8.3 <M	20.4 >M
DCM CD8a-	211.3 >3M	374.5 >3M	4.6 ~M	58.0 >M	4.6 ~M	184.5 >3M	772.5 >30M	4.6 ~M	4.6 ~M	894.5 >3M	4.6 <M	8.9 ~M	56.4 >3M
DP B220+	404.4 >3M	159.2 >M	4.6 ~M	29.1 >M	4.6 ~M	164.4 >3M	59.3 >3M	4.6 ~M	4.6 ~M	15.5 <M	5.0 >M	9.0 ~M	27.2 >M
Gr mac1+gr1+	204.2 >3M	86.5 <M	349.8 >30M	51.6 >M	4.6 ~M	170.3 >3M	11.8 ~M	4.6 ~M	8.0 >M	1018.0 >3M	22.2 >3M	8.3 <M	21.1 >M
Stem cells HSC	269.2 >3M	146.7 >M	23.0 >3M	13.5 <M	4.6 ~M	164.4 >3M	11.8 ~M	4.6 ~M	4.6 ~M	5.3 <M	5.0 ~M	15.5 >M	65.4 >3M
Macrophage bone marrow 0hr	144.8 >M	89.9 <M	4.6 ~M	17.6 <M	4.6 ~M	143.9 >3M	12.7 >M	4.6 ~M	4.6 ~M	80.1 <M	4.6 <M	8.3 <M	11.3 <M
Mast cells	1299.2 >10M	135.2 >M	3135.7 >30M	35.6 >M	4.8 ~M	266.7 >3M	11.7 ~M	4.6 ~M	4.6 ~M	15743.0 >30M	4.6 <M	8.3 <M	25.4 >M
Mega erythrocyte progenitor	97.2 >M	110.9 >M	13.9 >3M	15.4 <M	4.6 ~M	300.5 >10M	15.4 >M	4.6 ~M	4.6 ~M	12.8 <M	7.9 >M	19.9 >M	29.6 >M
Microglia	34.9 <M	63.1 <M	4.6 ~M	31.7 >M	4.6 ~M	102.3 >3M	11.8 ~M	4.6 ~M	4.6 ~M	10278.0 >30M	4.6 <M	8.3 <M	6.0 <M
Osteoclasts	26.9 <M	81.7 <M	4.6 ~M	25.7 >M	4.6 ~M	156.5 >3M	12.0 ~M	4.6 ~M	4.6 ~M	2237.4 >10M	6.2 >M	19.7 >M	15.1 ~M
T-cells CD4+	62.1 <M	266.3 >M	4.6 ~M	33.6 >M	4.6 ~M	145.6 >3M	11.8 ~M	4.6 ~M	4.6 ~M	4.8 <M	5.0 ~M	8.9 ~M	75.8 >3M
T-cells CD8+	56.0 <M	395.4 >3M	4.6 ~M	26.6 >M	4.6 ~M	150.2 >3M	12.4 >M	4.6 ~M	6.0 >M	8.9 <M	4.6 <M	8.3 <M	78.4 >3M
T-cells foxP3+	108.6 >M	95.9 <M	4.6 ~M	15.0 <M	4.6 ~M	110.7 >3M	52.0 >3M	4.6 ~M	4.9 >M	49.5 <M	6.7 >M	10.4 >M	140.8 >3M

Gene symbol	<i>Ptx4</i>	<i>Ephx3</i>	<i>H2-Ab1</i>	<i>Lst1</i>	<i>H2-Q2</i>	<i>Trem12</i>	<i>Olfr114</i>	<i>H2-Q1</i>	<i>H2-M5</i>	<i>Olfr113</i>	<i>F830016B08Rik</i>	<i>Alpk2</i>	<i>Megf10</i>
<b>Chromosome</b>	17	17	17	17	17	17	17	17	17	17	18	18	18
gene ID: MGI	1915759	1919182	103070	1096324	95931	2147038	2177497	95928	95917	2177496	3588218	2449492	2685177
Gene ID: NCBI	68509	71932	14961	16988	15013	328833	258284	15006	240095	258286	240328	225638	70417
Median	4.6	5.9	18.1	60.6	4.6	12.4	295.0	450.0	78.1	128.4	161.0	4.6	7.1
<b>Organs</b>													
Bone marrow	4.6~M	5.9>M	754.1>30M	1368.7>10M	8.9>M	116.7>3M	398.9>M	432.6<M	83.1>M	197.8>M	222.5>M	4.6~M	7.0~M
Liver	4.6~M	5.9>M	300.5>10M	72.6>M	13.4>M	12.4~M	384.3>M	889.9>M	82.0>M	132.6>M	188.8>M	4.6~M	7.0~M
Lymph nodes	4.6~M	6.6>M	18340.6>30M	1023.7>10M	7.1>M	63.6>3M	318.0>M	1380.9>3M	82.0>M	149.4>M	168.5>M	4.6~M	6.3<M
Spleen	4.6~M	5.8~M	18036.7>30M	1169.1>10M	7.1>M	104.2>3M	866.3>M	668.5>M	94.4>M	160.7>M	239.3>M	5.9>M	6.6<M
<b>Cells</b>													
B-cells MZ	4.6~M	5.9~M	1661.3>30M	58.1~M	7.1>M	26.7>M	N/A	N/A	N/A	N/A	N/A	25.0>3M	7.0~M
CMP	4.6~M	5.9~M	21.7>M	398.9>3M	7.1>M	20.5>M	N/A	N/A	N/A	N/A	N/A	4.6~M	7.0~M
DCL CD8a+	4.6~M	5.9~M	5460.4>30M	549.2>3M	7.1>M	11.7<M	N/A	N/A	N/A	N/A	N/A	4.6~M	13.1>M
DCM CD8a-	4.6~M	5.9~M	16091.3>30M	4579.7>30M	7.1>M	12.4~M	N/A	N/A	N/A	N/A	N/A	11.7>M	7.1~M
DP B220+	6.4>M	8.2>M	3018.5>30M	279.3>3M	7.1>M	13.6>M	265.2<M	1939.3>3M	76.4~M	147.2>M	152.8<M	4.6~M	7.0~M
Gr mac1+gr1+	4.6~M	6.0~M	19.8>M	4046.1>30M	15.3>3M	123.0>3M	N/A	N/A	N/A	N/A	N/A	4.6~M	21.3>M
Stem cells HSC	4.6~M	5.9~M	23.3>M	880.2>10M	7.1>M	12.4~M	N/A	N/A	N/A	N/A	N/A	4.6~M	7.1~M
Macrophage bone marrow 0hr	4.6~M	5.2<M	40.8>M	3009.6>30M	13.9>3M	7.7<M	N/A	N/A	N/A	N/A	N/A	4.6~M	5.1<M
Mast cells	4.6~M	5.9~M	9.5<M	2552.0>30M	9.9>M	12.4~M	324.7>M	515.7>M	80.9>M	141.6>M	165.2>M	67.9>10M	4.6<M
Mega erythrocyte progenitor	4.6~M	5.9~M	13.9<M	101.9>M	7.1>M	21.7>M	N/A	N/A	N/A	N/A	N/A	4.6~M	8.2>M
Microglia	4.6~M	5.9~M	9.5<M	555.7>3M	52.2>10M	12.4~M	N/A	N/A	N/A	N/A	N/A	4.6~M	53.3>3M
Osteoclasts	4.6~M	5.9~M	424.3>10M	601.6>3M	7.1>M	12.4~M	289.9<M	2244.9>3M	78.7>M	130.3>M	162.9>M	4.6~M	7.0~M
T-cells CD4+	4.6~M	5.9~M	11.1<M	52.9<M	7.1>M	24.8>M	313.5>M	2150.6>3M	79.8>M	139.3>M	164.0>M	4.6~M	7.0~M
T-cells CD8+	4.6~M	5.9~M	16.2<M	80.7>M	7.1>M	12.4~M	338.2>M	1777.5>3M	80.9>M	139.3>M	168.5>M	4.6~M	7.0~M
T-cells foxP3+	4.6~M	8.3>M	172.7>3M	122.9>M	8.1>M	15.2>M	N/A	N/A	N/A	N/A	N/A	4.6~M	7.0~M

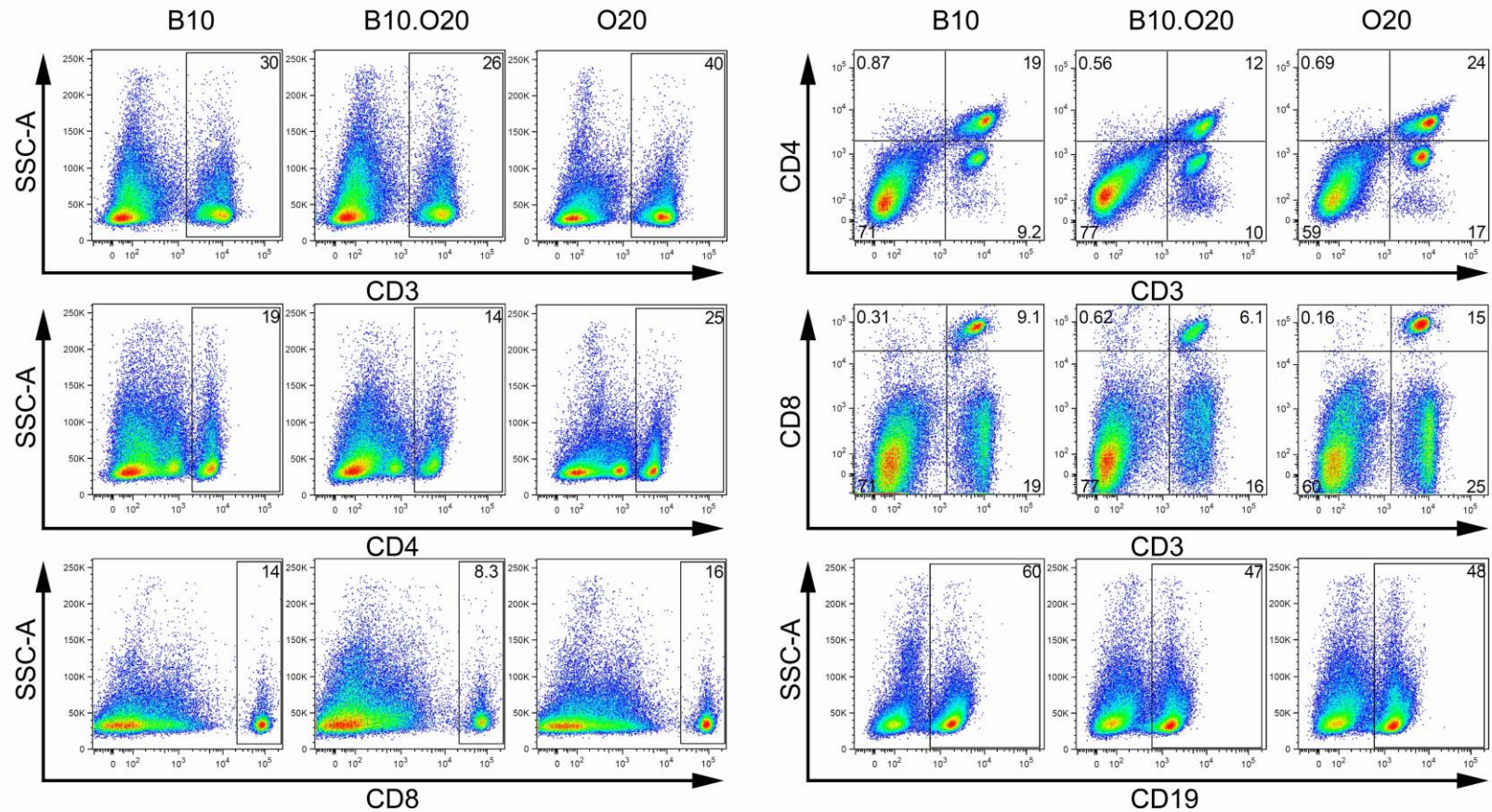
**Abbreviations:** MZ: Marginal zone; CMP: common myeloid progenitor; DCL: Dendritic cells lymphoid; DCM: Dendritic cells myeloid; DP: Dendritic Plasmacytoid; Gr: Granulocytes; HSC: Hematopoietic stem cells; Mac. BM: Macrophage Bone marrow; MEP: Mega erythrocyte progenitor; N/A: Not assessed. In **bold**: three fold or higher expression. Data were compiled from public database BioGPS (<http://biogps.org>) July 7, 2019. First column: relative units; Second column: relationship to median (M); M=median value across all samples for a single probe set. Color scale: blue: lower than median, gray: similar to median, yellow to dark orange: higher than median (the intensity of yellow color is relative to the expression level as indicated). No data was found for: *Btm4*, *Btm6*, *AU023871*, *Gm19684*, *2410017117Rik*, *Gm8909*, *Esp31*, *Esp36*, *Gm4841*

**Supplementary Figure 1. Genetic influence on frequency of myeloid cell subsets.** Flow cytometric analysis of spleens of representative mice of strains B10, B10.O20 and O20 shows internal cell complexity measured by SSC-A (side scatter) and CD11b, CD40, F4/80, CD14 cell surface marker status or Gr1/CD11b cell surface marker status of individual cells.

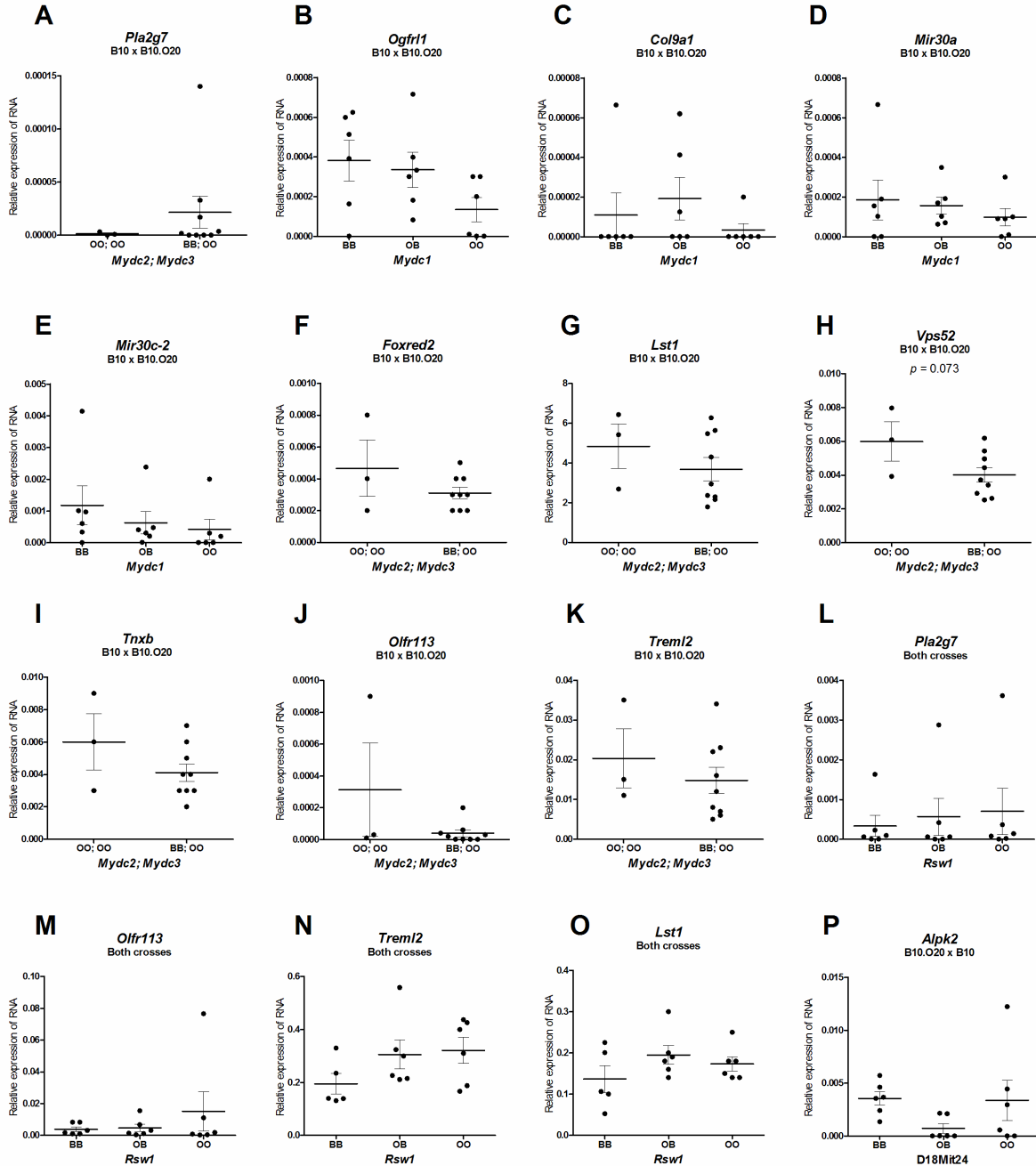




**Supplementary Figure 2 Genetic influence on frequency of lymphoid cell subsets.** Flow cytometric analysis of spleens of representative mice of strains B10, B10.O20 and O20 shows internal cell complexity measured by SSC-A (side scatter) and CD3, CD4, CD8, CD1 cell surface marker status, and CD4/CD3 or CD8/CD3 cell surface marker status of individual cells.



**Supplementary Figure 3: Expression of mRNA of potential candidate genes in spleen of F<sub>2</sub> mice.** Relative expression of a target gene versus a reference gene *Gapdh* is shown. Statistical analysis was performed by ANOVA followed by Bonferroni multiple comparison test or by two-tailed unpaired t test. *P* values are not significant (>0.05). Bars represent the average  $\pm$  SEM.



## REFERENCES

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