

SUPPLEMENTAL MATERIAL

**Identification of a Unique TGF- β Dependent Molecular and Functional
Signature in Microglia**

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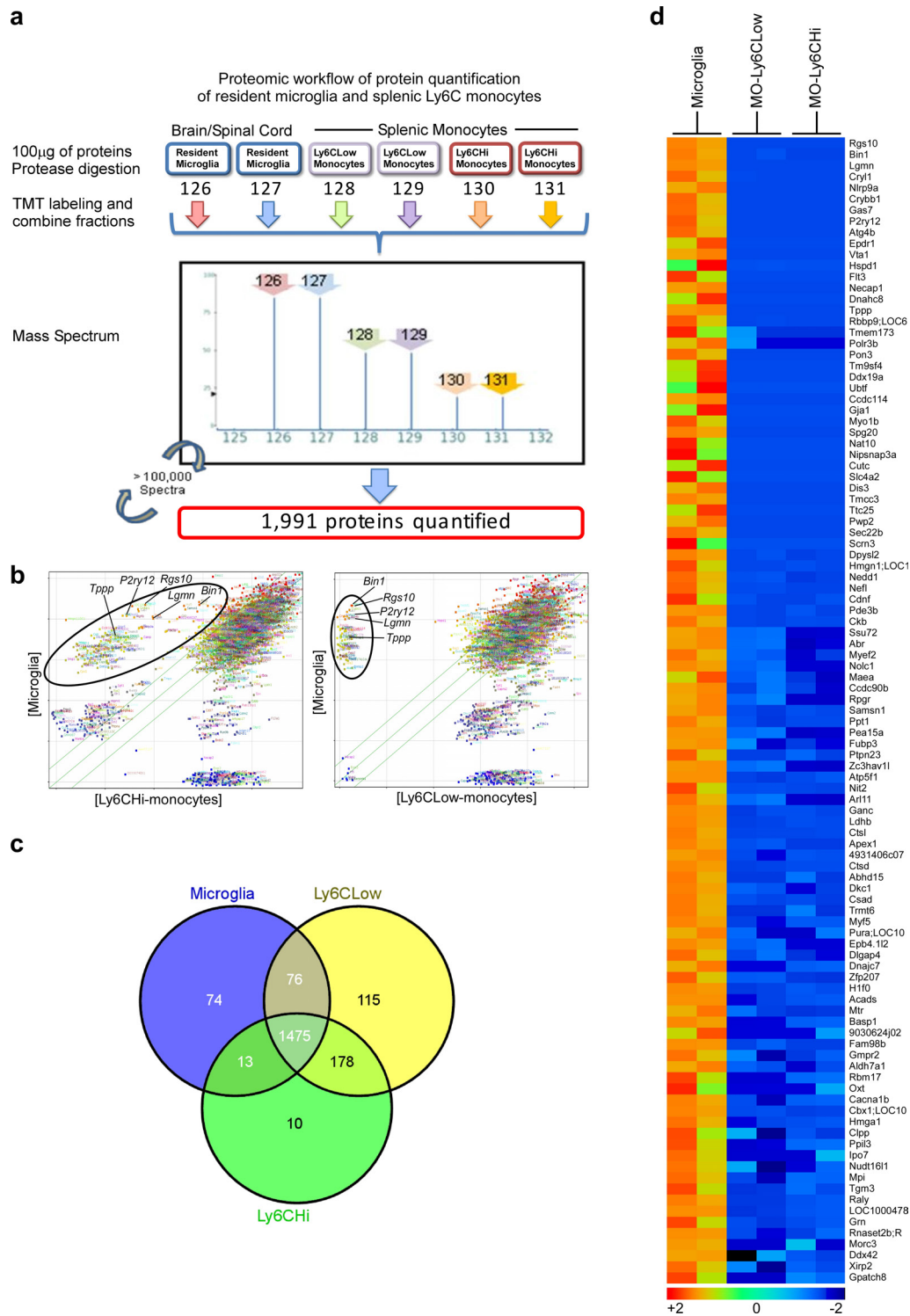
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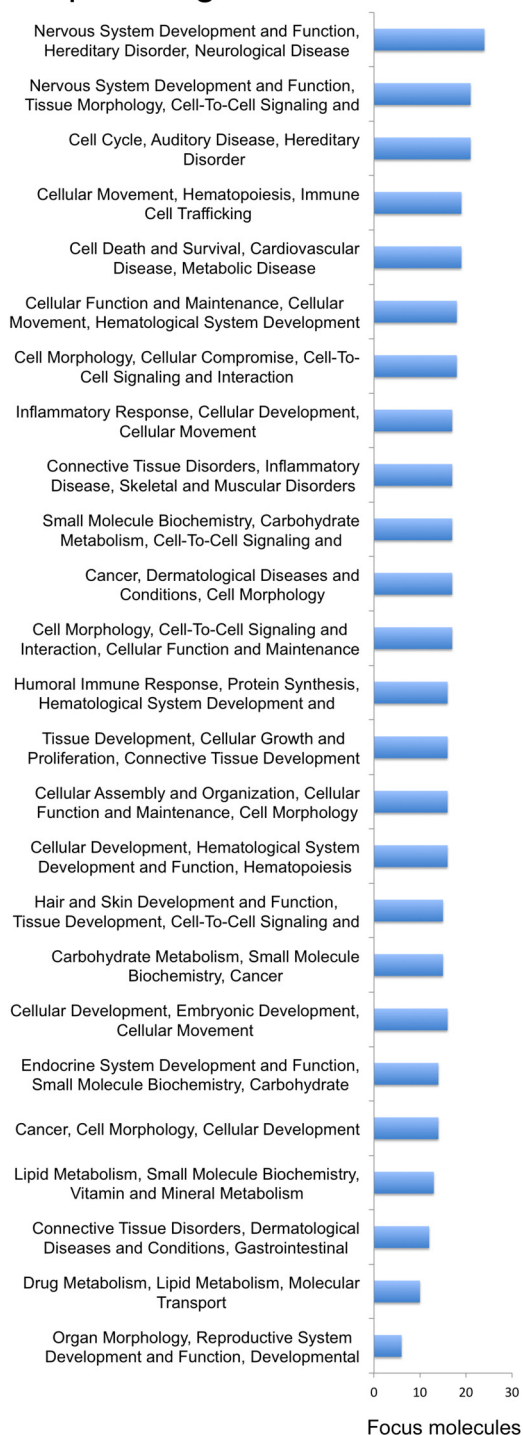
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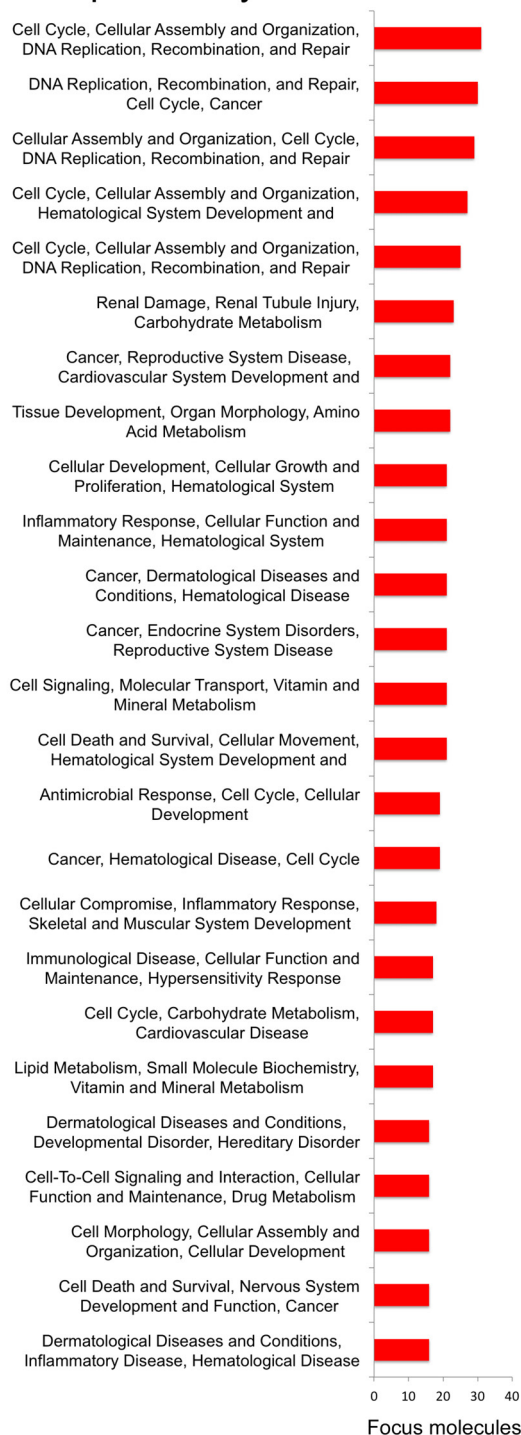


Supplementary Figure 1. Identification of protein signature in microglia and Ly6C monocyte subsets. (a) Schematic representation of the workflow for TMT-based quantitative proteomic analysis of microglia and splenic Ly6C monocytes. (b) Protein expression scatter plot of microglia versus monocytes subsets. (c) Venn diagram of unique and common proteins in microglia vs. Ly6C^{Hi} and Ly6C^{Low} monocytes. (d) Heatmap of 103 enriched microglia proteins (>5-fold).

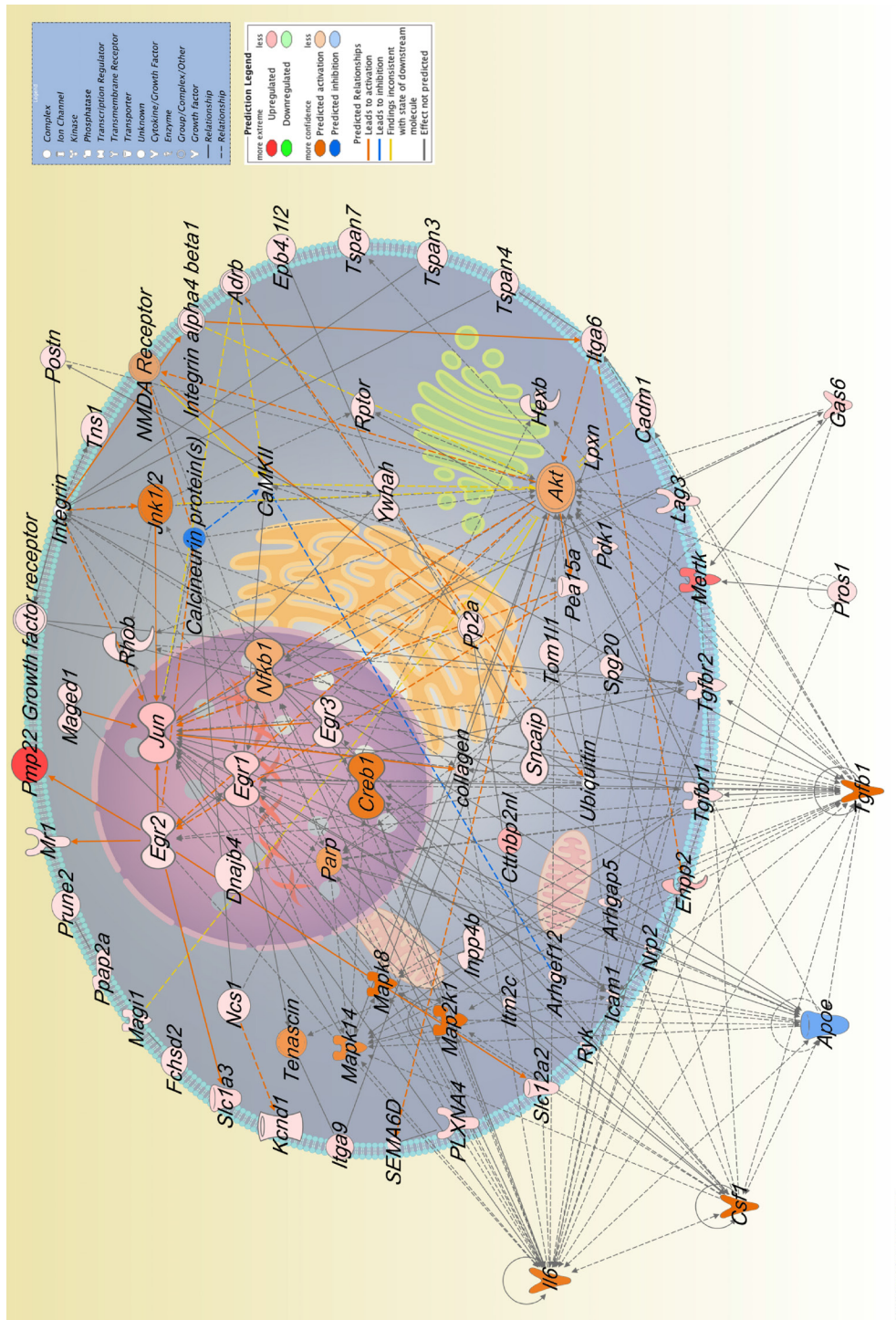
Top microglia functions



Top monocyte functions

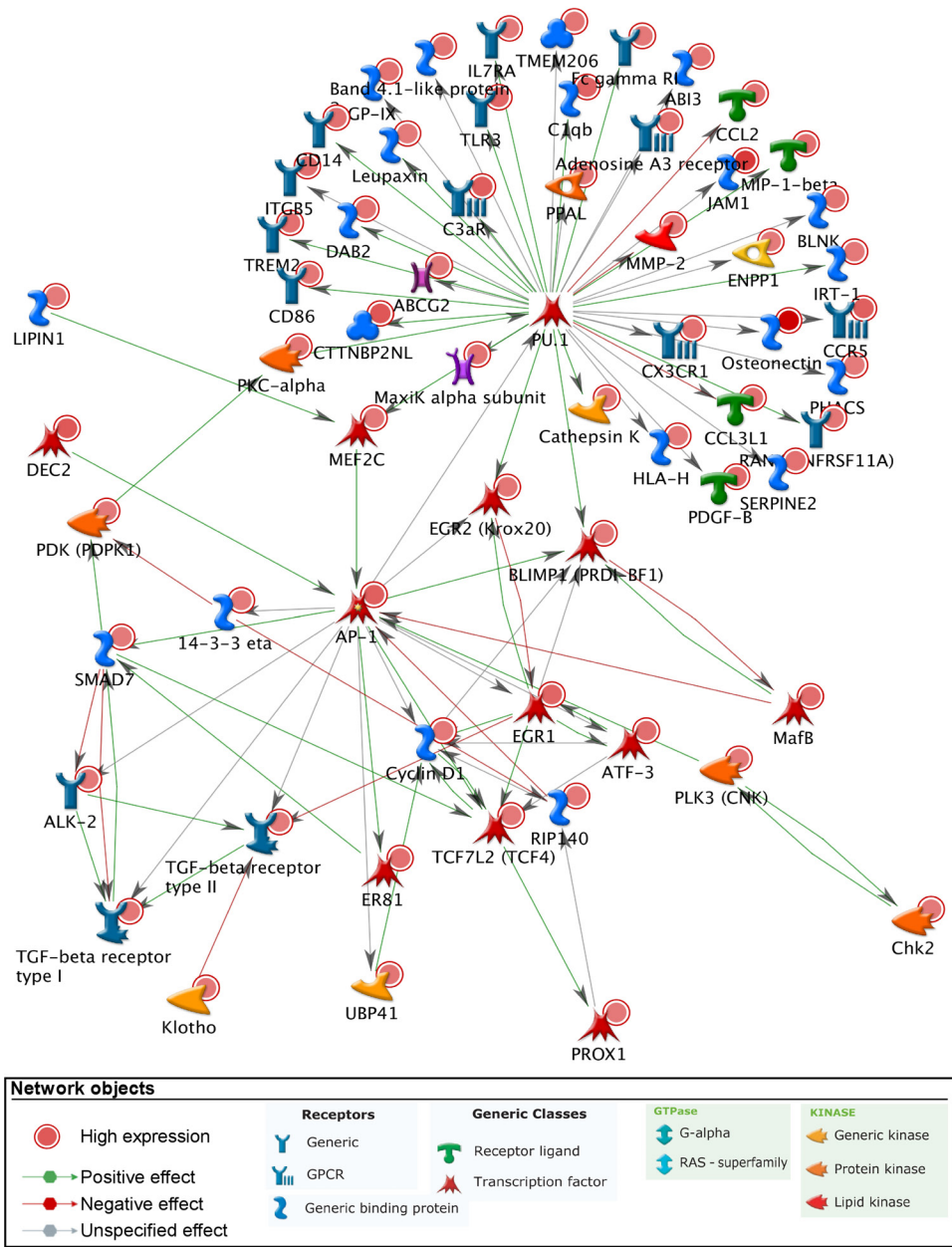


Supplementary Figure 2. Top biological functions in microglia. Microglia and monocyte gene signature identified by AffyExon1 arrays (see Fig. 1a) were analyzed by Ingenuity pathway analysis (IPA™). Bars indicate molecules present in dataset for each function.



Supplementary Figure 3. Nervous system development and function in microglia. The subcellular localization of top microglial functions genes from Supplementary Figure 2 (Nervous system development and function, hereditary disorders, neurological disease genes) are illustrated. For each molecule in the dataset the expression fold change as compared to monocytes, P value and normalized expression level are presented.

Microglial PU.1 network

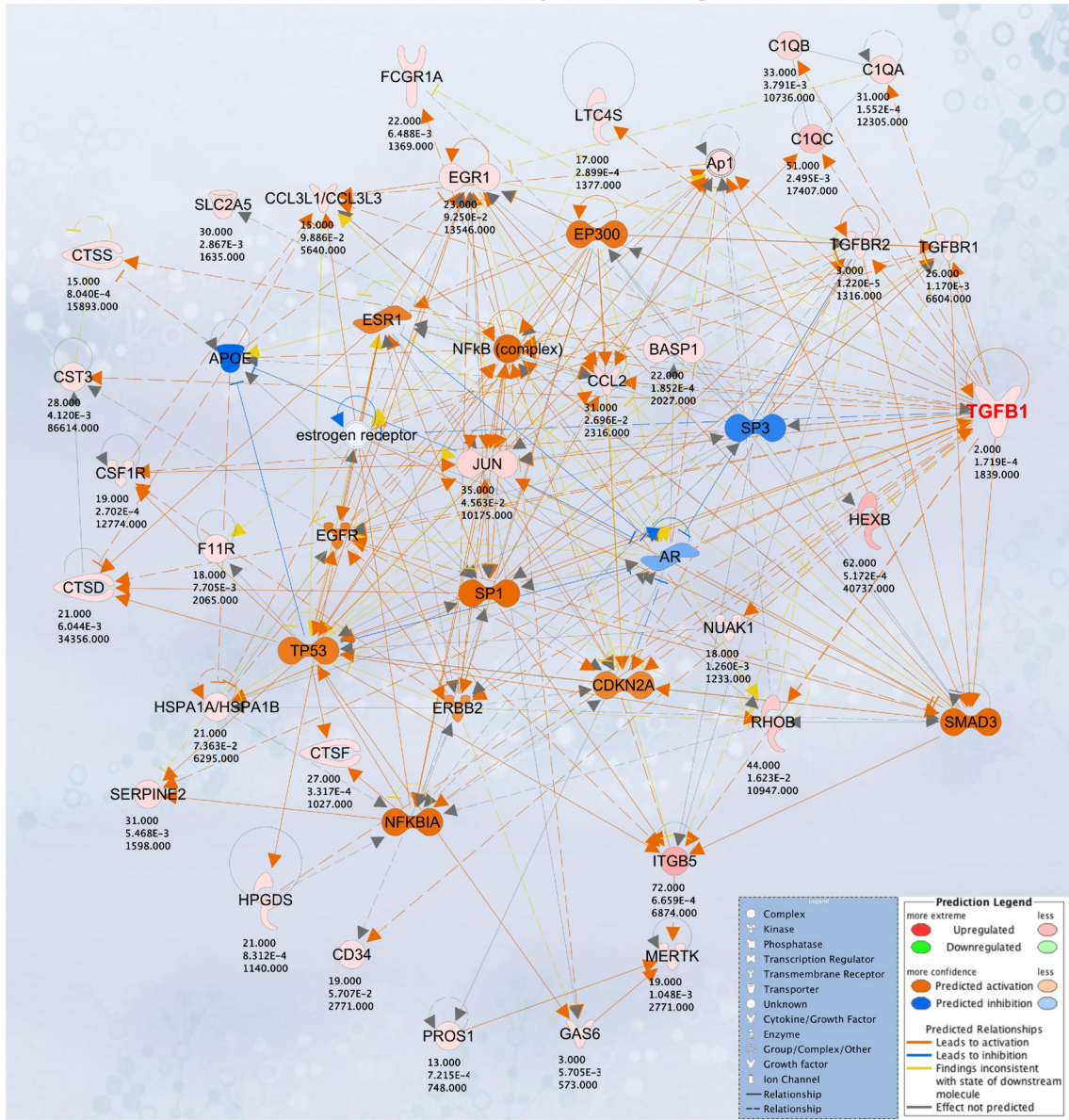


Supplementary Figure 4. Top microglial interactions by protein function. Illustration of microglial PU.1 network.

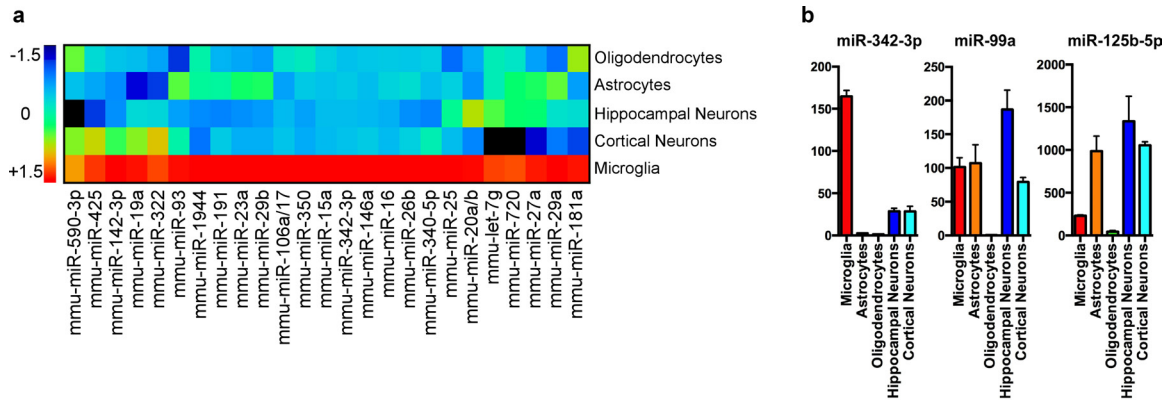


Supplementary Figure 5. Canonical pathways in microglia and monocytes. Microglial and monocytes gene signatures identified with AffyExon1 arrays were analyzed by IPA™ for canonical pathways. Bars indicate $-\log P$ value (ratio of molecules present in the dataset out of all the function related molecules).

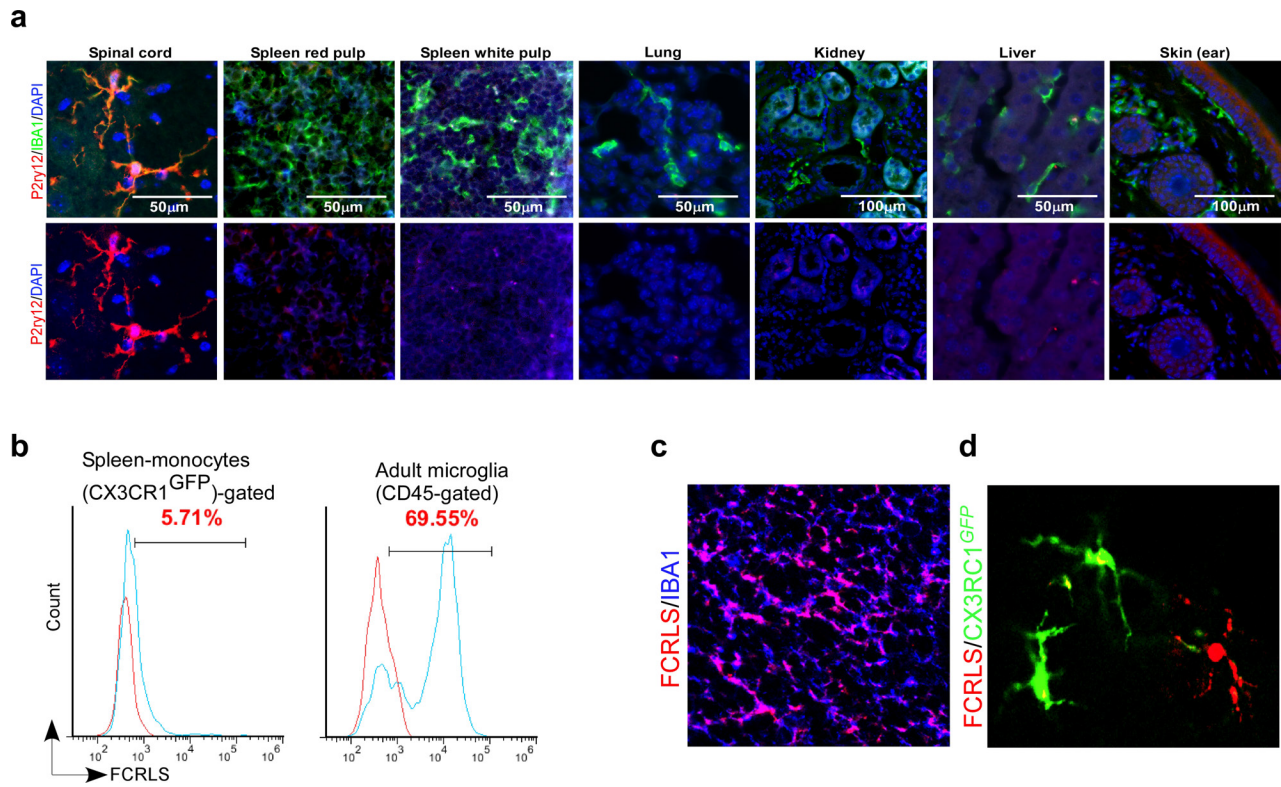
TGFβ pathway in microglia



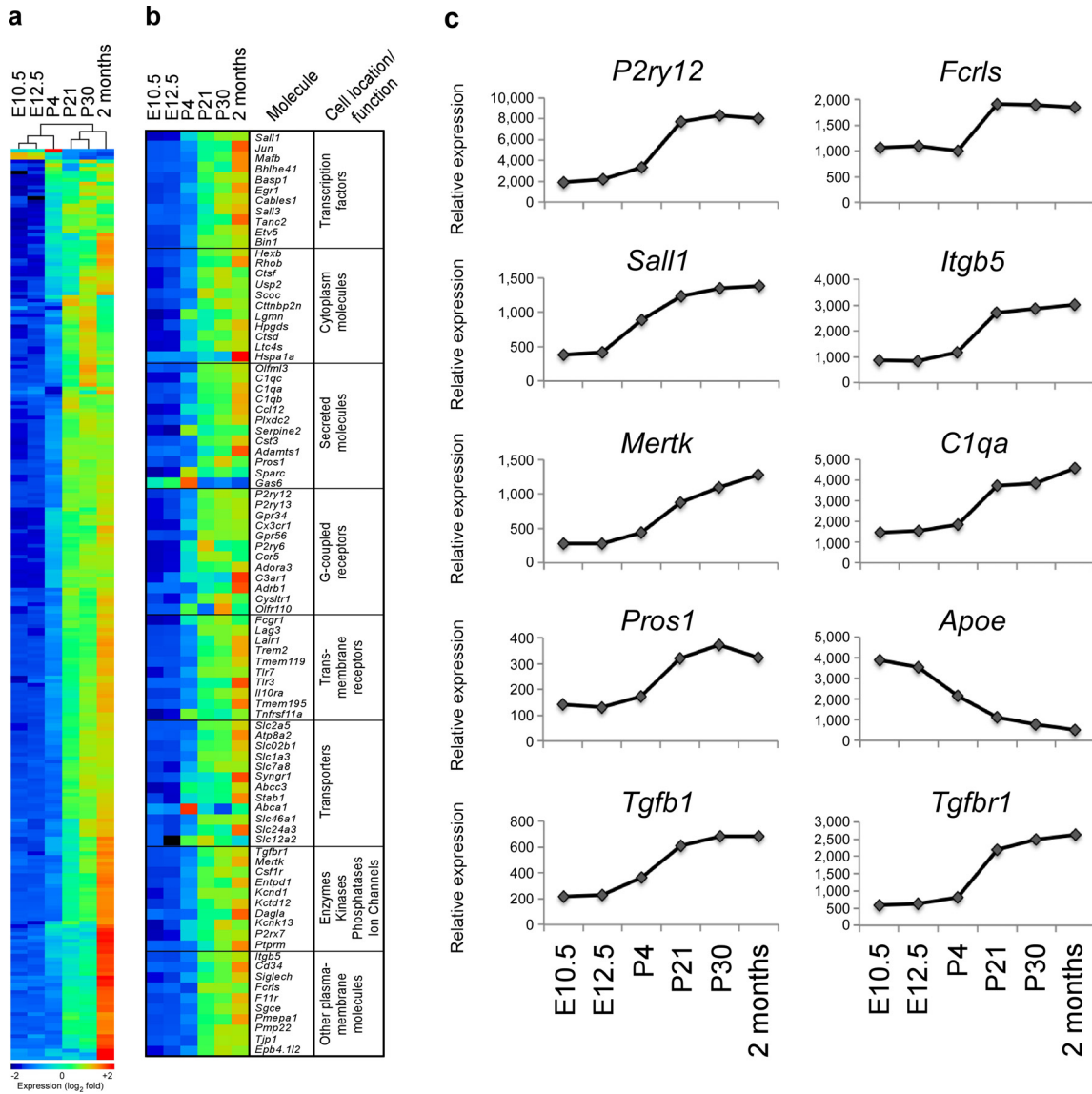
Supplementary Figure 6. TGF-β pathway in microglia. For each molecule in the dataset the expression fold change as compared to monocytes, P value and normalized expression level are presented.



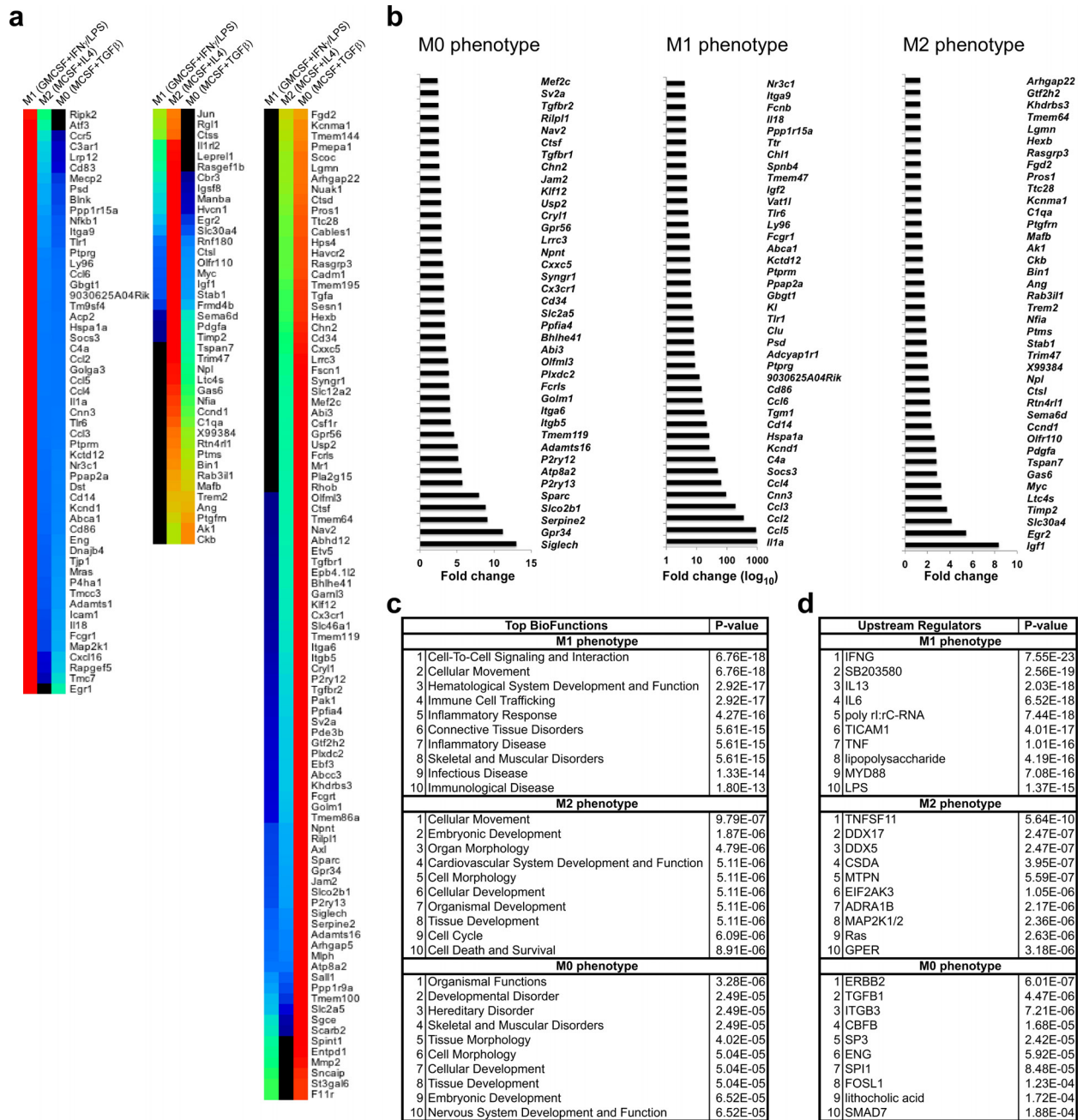
Supplementary Figure 7. miRNA profile in microglia vs. astrocytes, oligodendrocytes and neurons. (a) Heatmap of biological duplicates for FCRLS⁺ adult microglia (n = 5 mice), Glt-EGFP⁺ adult astrocytes (n = 9 mice), adult oligodendrocytes (n = 5 mice) and primary postnatal hippocampal and cortical neurons. Top 25 enriched miRNAs in microglia are presented (full miRNA list, [Source data – Supplementary Figure 7](#)). Each lane represents the average expression value of two biological duplicates per cell type. (b) qPCR analysis of microglia enriched miRNAs (miR-342-3p, miR-99a and miR-125b-5p) in CNS cell type. miRNA expression level was normalized against U6 miRNA using ΔCt . Bars show mean \pm SEM. Shown is one of two individual experiments.



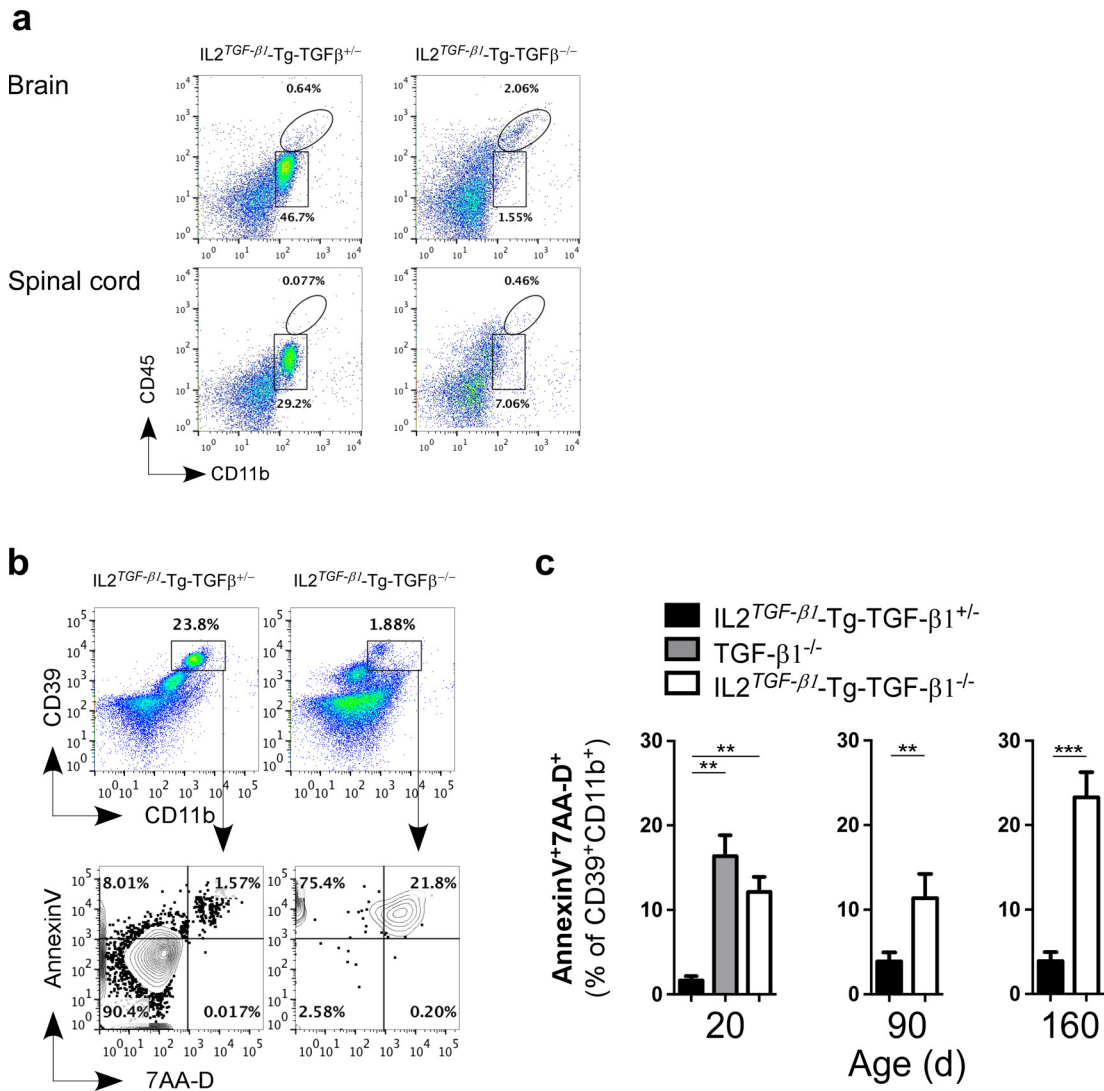
Supplementary Figure 8. Specificity of P2ry12 and FCRLS antibodies in resident microglia. (a) Immunohistochemical analysis of mouse spinal cord, spleen red and pulp, lung, kidney, liver and skin (ear) stained with anti-P2ry12 (microglia; red), anti-Iba-1 (myeloid cells; green) and DAPI (nucleus; blue). Representative images of 5 mice. (b) FACS analysis of FCRLS surface expression in splenic CX3CR1^{GFP/+} monocytes and CD11b/CD45⁺ brain microglia. (c and d) Confocal images of mouse brain stained with Iba-1 and polyclonal FCRLS antibody in (c) naïve and (d) chimeric CX3CR1^{GFP/+} mice. Anti-FCRLS signal co-localized with Iba-1⁺ microglia and does not stain recruited monocytes in the brain of CX3CR1^{GFP} chimeric mouse transplanted with bone marrow derived cells from CX3CR1^{GFP/+} transgenic mice.



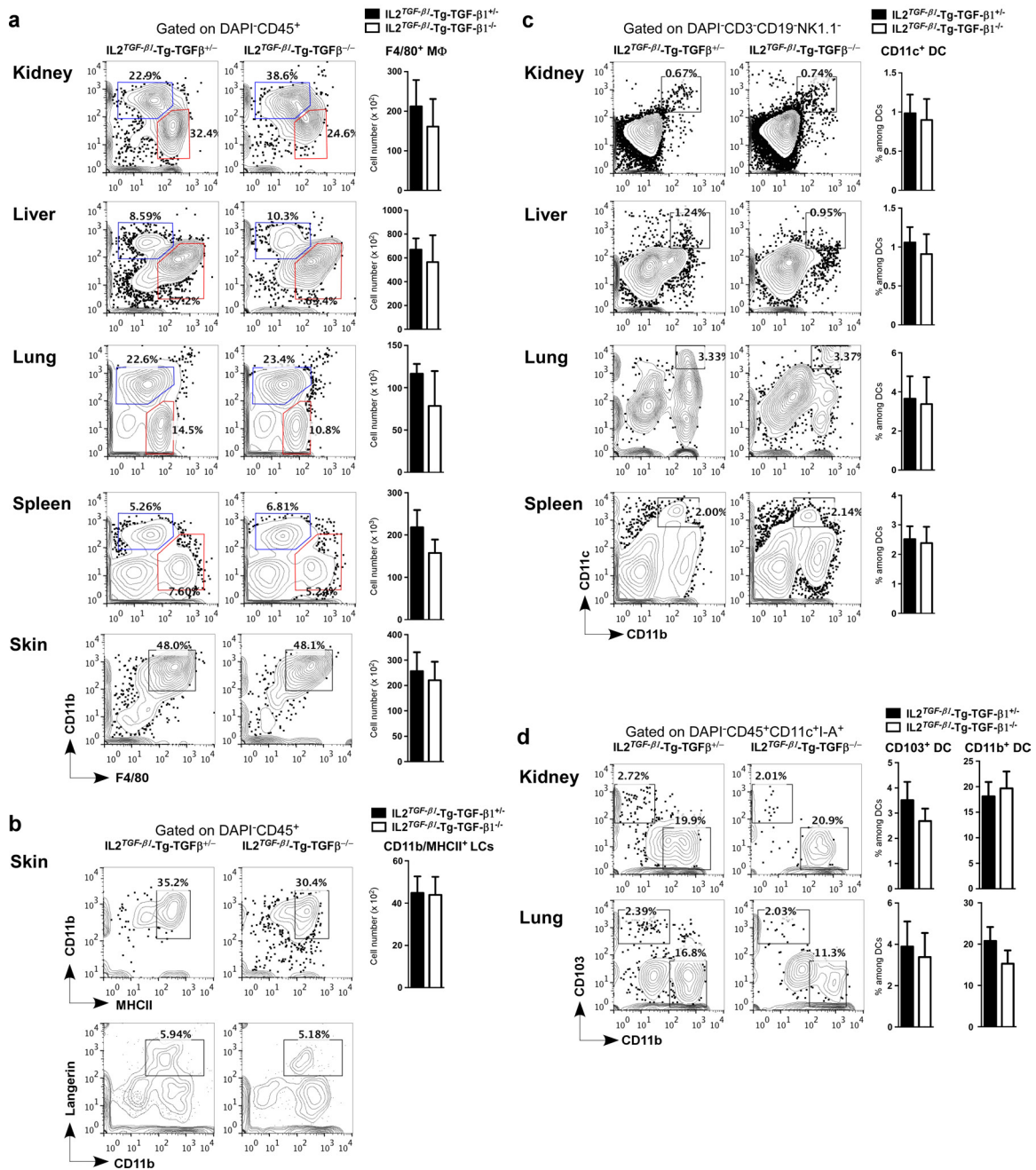
Supplementary Figure 9. Microglia signature during development. **(a)** MG400 expression profile of microglia from mice brain at E10.5, E12.5, P3, P21, P30 and 2 months of age (full gene list, [Source data – Supplementary Figure 9](#)). Results were log-transformed, normalized (to the mean expression of zero across samples) and centered, and populations and genes were clustered by pairwise centroid linkage with the Pearson correlation. Data are pooled of 2 different experiments; E10.5 ($n = 10$), E12.5 ($n = 10$), P4 ($n = 8$), P21 ($n = 5$), P30 ($n = 5$) and 2 months ($n = 5$). **(b)** Top microglial molecules grouped according to cell localization and function. **(c)** qPCR analysis of 6 selected microglia genes in MCSF+TGF- β 1 cultured microglia. Gene expression level was normalized against *Gapdh* using Δ Ct.



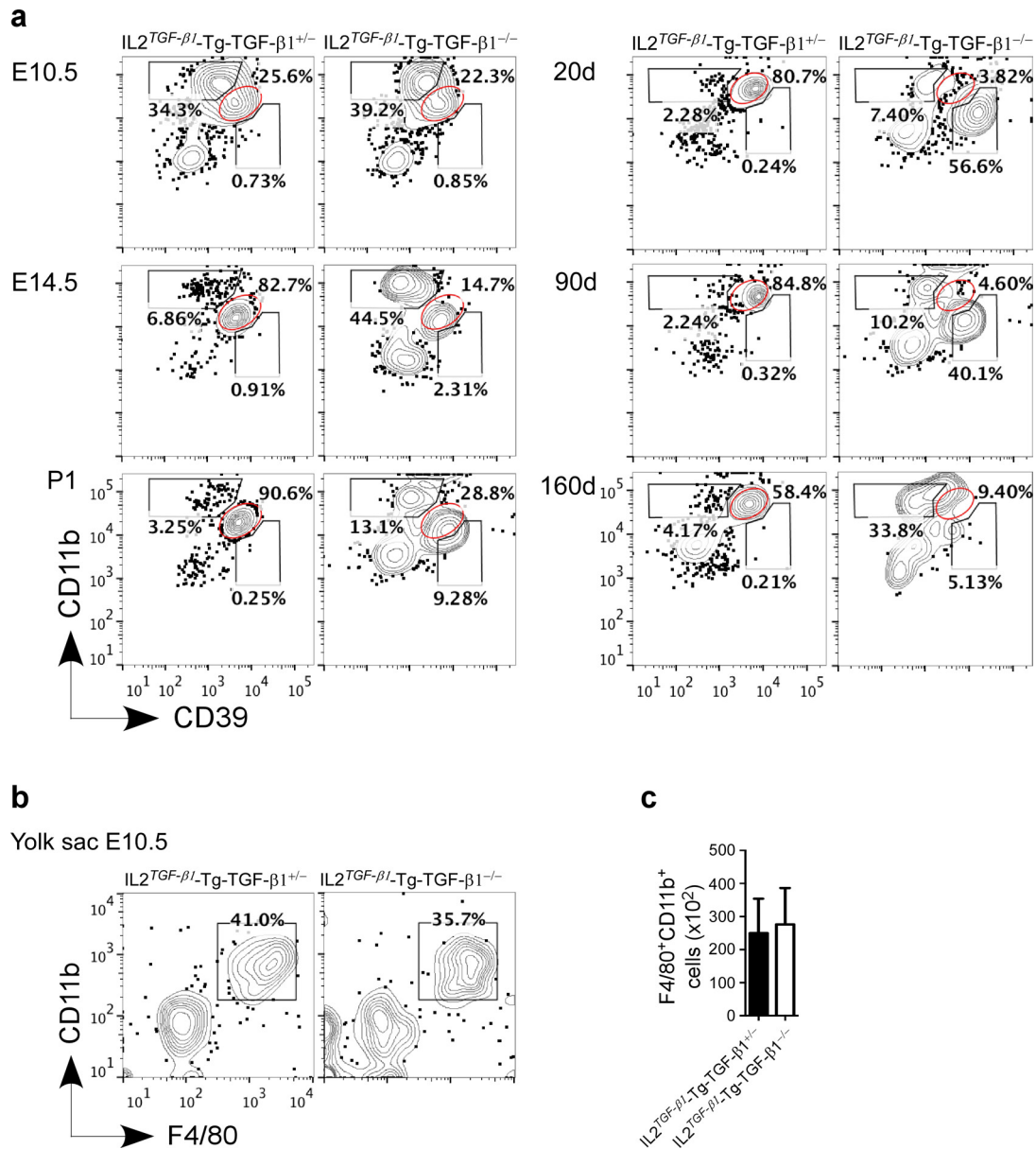
Supplementary Figure 10. M0, M1 and M2 microglial phenotypes as measured by MG400 chip. (a) Heatmap of significantly affected MG400 genes in M0, M1 and M2 polarized microglia. One representative of three individual experiments is shown. (b) Top 40 affected genes in M0, M1 and M2 microglia. Bars represent fold change as compared to the other two phenotypes. (c and d) IPA™ analysis of (c) top bio functions and (d) Top upstream regulators in M0-, M1- and M2-polarized microglia.



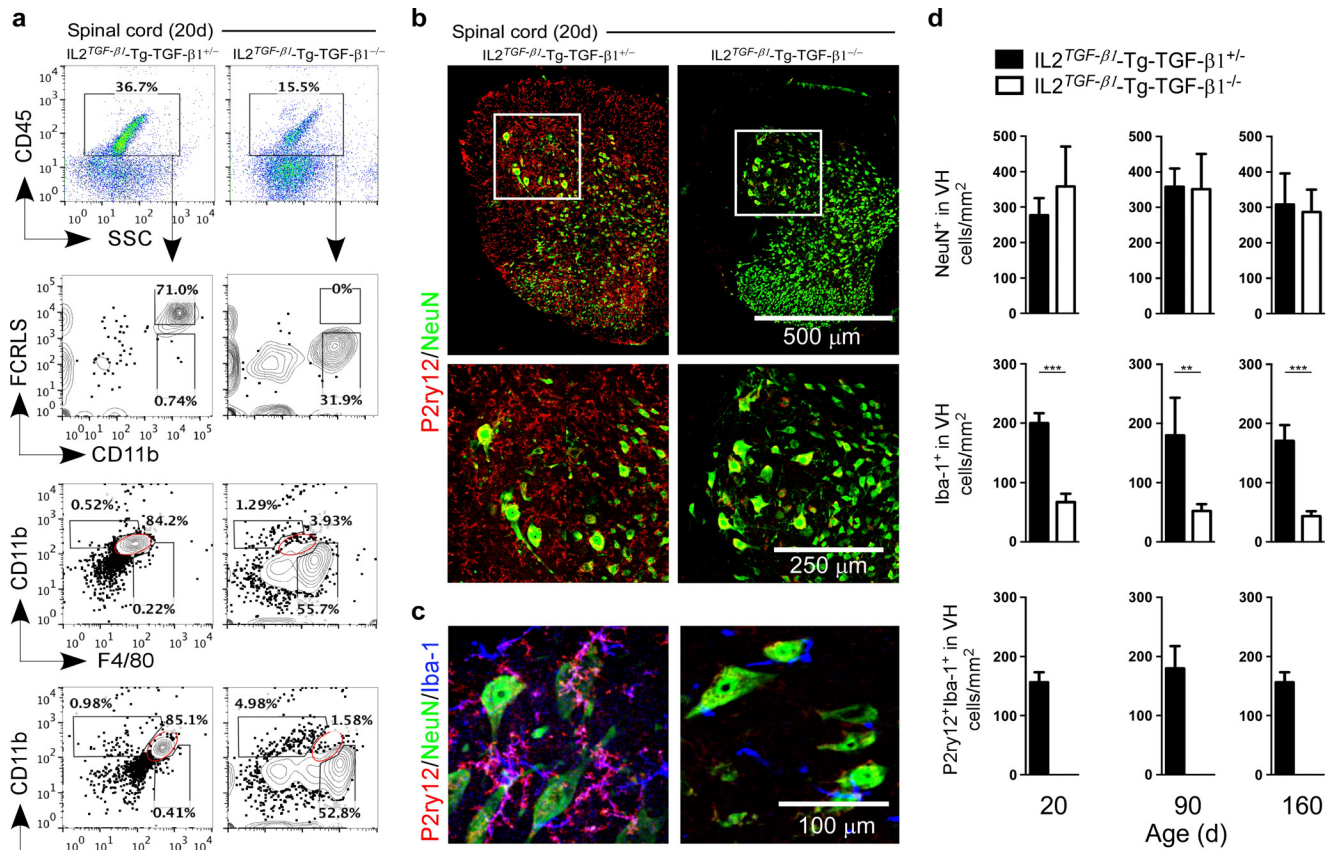
Supplementary Figure 11. Microglia loss in CNS-TGFβ1^{-/-} mice. (a) Representative FACS analysis of isolated brain- and spinal cord-derived mononuclear cells stained with CD45 and CD11b antibodies at 160d of age in IL2^{TGFβ1}-Tg-TGF-β1^{+/-} (n = 6) and IL2^{TGFβ1}-Tg-TGF-β1^{-/-} (n = 6) mice. (b and c) Increased apoptosis of CD39⁺CD11b⁺ cells in the brain of CNS-TGF β 1^{-/-} mice. (b) Representative FACS analysis of isolated brain-derived mononuclear cells for apoptosis as measured by AnnexinV and 7AA-D in CD39⁺CD11b⁺-gated cells at 160d of age in IL2^{TGFβ1}-Tg-TGF-β1^{+/-} (left) and IL2^{TGFβ1}-Tg-TGF-β1^{-/-} (right) mice. (c) Quantitative analysis of AnnexinV⁺7AA-D⁺ cell as percentage of CD39⁺CD11b⁺ cells in TGF-β1^{-/-}, IL2^{TGF-β1}-Tg-TGF-β1^{+/-} and IL2^{TGF-β1}-Tg-TGF-β1^{-/-} mice at 20 (n = 6), 90 (n = 5) and 160 (n = 5) days. Data represent mean ± s.e.m. **P<0.01, F_{2,6}=2.146 1-Way ANOVA followed by Dunnett's multiple-comparison *post-hoc* test for comparison at 20d and **P<0.01, t=4.51 and ***P<0.001, t=13.84; Student's *t* test, 2-tailed for comparison at 90d and 160d.



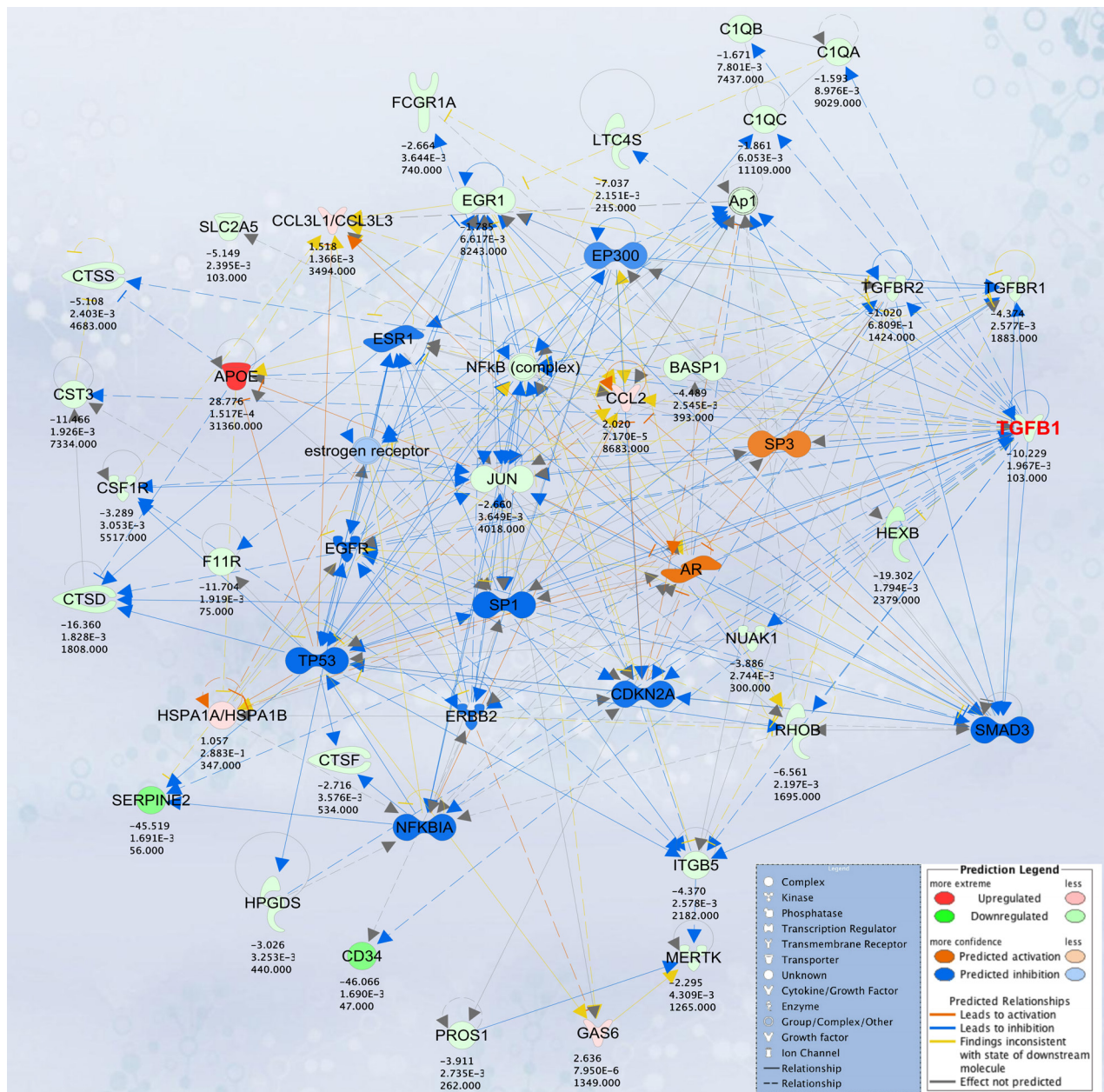
Supplementary Figure 12. Macrophages, dendritic cells and Langerhans cells are not affected in peripheral organs of CNS-TGFβ1^{-/-} mice. (a-d) Nonlymphoid and lymphoid tissue myeloid cells isolated from IL2^{TGFβ1}-Tg-TGF-β1^{+/-} (left) and IL2^{TGFβ1}-Tg-TGF-β1^{-/-} (right) mice at 160d were analyzed by flow cytometry. FACS representative dot plots show the percentage and absolute numbers of (a) kidney, liver, lung, spleen and skin derived CD11b⁺F4/80⁺ macrophages and (b) Langerhans cell (LC) stained with MHCII⁺CD11b⁺ and Langerin⁺CD11b⁺ in the ear skin cell suspension among DAPI⁻CD45⁺ cells of IL2^{TGFβ1}-Tg-TGF-β1^{+/-} (n = 6) and IL2^{TGFβ1}-Tg-TGF-β1^{-/-} (n = 6) mice. (c) Plots show percentage of CD11c⁺ DCs among gated DAPI⁻CD3⁻CD19⁻NK1.1⁺ cells. (d) Dot plots show percentage of CD103⁺ and CD11b⁺ DCs among gated DAPI⁻CD45⁺CD11c⁺I-A⁺ cells. Bars represent data from 2 pooled experiments. Errors bars represent ± s.e.m.



Supplementary Figure 13. Loss of microglia during development in CNS-TGF-β1 deficient mice. (a) FACS analysis of CD39 and CD11b expression among CD45⁺ cells in the brain during development and aging in IL2^{TGF-β1}-Tg-TGF-β1^{+/-} and IL2^{TGF-β1}-Tg-TGF-β1^{-/-} mice at E10.5 (n = 4), E14.5 (n = 5), P1 (n = 5), 20d (n = 6), 90d (n = 5), 160d (n = 5). **(b)** FACS plots show the percentage among CD45⁺ cells and **(c)** total cell number ± s.e.m. of F4/80⁺CD11b⁺ primitive macrophages in the yolk sac at E10.5 in IL2^{TGF-β1}-Tg-TGF-β1^{+/-} (n = 6) and IL2^{TGF-β1}-Tg-TGF-β1^{-/-} (n = 10) mice. $P=0.74$, $t=0.35$ Student's *t* test, 2-tailed.



Supplementary Figure 14. Microglia loss in the spinal cord of CNS-TGFβ1^{-/-} mice. (a) Representative FACS analysis of isolated spinal cord-derived mononuclear cells stained for FCRLS, F4/80, CD39 and CD11b among hematopoietic (CD45⁺) cells at 20d of age in IL2^{TGF-β1}-Tg-TGF-β1^{+/-} and IL2^{TGF-β1}-Tg-TGF-β1^{-/-} mice. Immunohistochemical analysis of mouse spinal cord axial section of lumbar level stained with (b) anti-P2ry12 (microglia) and anti-NeuN (neurons) and (c) anti-P2ry12 (microglia), Iba-1 (myeloid cells) and anti-NeuN (neurons) at 20 days of age (IL2^{TGF-β1}-Tg-TGF-β1^{+/-} and IL2^{TGF-β1}-Tg-TGF-β1^{-/-}) mice. Representative images of 3-5 mice. Scale bar represents 500μm (top panel) and 250μm (zoomed are indicated, bottom panel). (d) Quantitative analysis of NeuN⁺, Iba-1⁺ and P2ry12⁺/Iba-1⁺ cells in IL2^{TGF-β1}-Tg-TGF-β1^{+/-} and IL2^{TGF-β1}-Tg-TGF-β1^{-/-} mice at 20, 90 and 160 days of age. Data represent mean ± s.e.m (n = 5). **P<0.01, ***P<0.001, Student's *t* test, 2-tailed.



Supplementary Figure 15. TGF- β pathway and downstream microglial molecules are suppressed in CNS-TGF β 1^{-/-} mice. For each molecule in the dataset the expression fold change as compared to microglia from IL2^{TGF- β 1}-Tg-TGF- β 1^{+/-} mice, P value and normalized expression level are presented.

Supplementary Table 1:
Top 25 enriched genes in each cell type based on hierarchical clustering

GeneName	Microglia	Astrocytes	Oligodendrocytes	Cort.Neurons	Hipp.Neurons
Oligodendrocytes					
<i>Enpp2</i>	17	307	13613	34	24
<i>Ptgsds</i>	10	52	4343	14	5
<i>Appl1</i>	15	976	11980	775	1130
<i>Ncam1</i>	4	881	1521	334	354
<i>Ttr</i>	10	98	1470	17	11
<i>Omg</i>	7	619	1366	157	76
<i>Gpm6b</i>	22	4040	4657	1000	1643
<i>Qdpr</i>	79	136	5210	136	213
<i>Slc12a2</i>	68	38	1295	36	20
<i>Kcnk13</i>	81	7	320	27	11
<i>Tmeff1</i>	11	19	457	126	109
<i>Chn2</i>	92	9	401	36	40
<i>App</i>	130	440	5319	564	785
<i>Dip2a</i>	14	53	411	29	29
<i>Tppp</i>	82	86	1641	116	194
<i>Gab1</i>	139	159	1160	46	60
<i>Kl</i>	16	20	200	23	7
<i>Slc4a2</i>	42	47	384	26	15
<i>Sv2a</i>	27	88	1025	251	252
<i>Tmcc3</i>	83	63	450	25	26
<i>Frm4b</i>	199	30	222	13	11
<i>Gas7</i>	9	146	350	240	201
<i>Bin1</i>	407	35	715	69	71
<i>Sema6d</i>	11	167	190	18	14
<i>Tmem144</i>	75	60	209	20	9
Astrocytes					
<i>Piprz1</i>	2	2144	104	397	546
<i>Clu</i>	8	7418	842	419	639
<i>Gpr3711</i>	12	3047	131	26	5
<i>Gpm6a</i>	10	3263	130	1305	1654
<i>Slc6a1</i>	6	1373	193	156	96
<i>Tmem47</i>	6	861	93	147	156
<i>Slc1a3</i>	257	16656	425	670	1266
<i>Alcb4</i>	5	643	295	276	323
<i>Nrcam</i>	6	349	19	146	268
<i>Apoe</i>	368	11630	2882	851	1672
<i>Ii18</i>	55	404	79	18	21
<i>Tspan7</i>	65	1428	120	184	280
<i>Chi3l1</i>	8	102	16	15	6
<i>Axl</i>	11	131	13	17	14
<i>Cables1</i>	102	142	9	21	15
<i>Ahcy1</i>	64	1017	324	152	190
<i>C4a</i>	9	120	51	16	33
<i>Adcyap1r1</i>	9	110	16	40	28
<i>Tlr3</i>	66	118	28	17	9
<i>Fcgrt</i>	139	172	54	22	14
<i>Phyh1</i>	132	602	105	90	118
<i>Ckb</i>	357	4334	2061	1070	1179
<i>Cpne2</i>	14	129	21	37	44
<i>Tmem100</i>	56	77	13	12	12
<i>Etv5</i>	183	437	40	131	137
Neurons					
<i>Nefl</i>	8	29	5	84	294
<i>Rtn1</i>	39	313	19	782	1126
<i>Chl1</i>	4	163	14	179	270
<i>Basp1</i>	535	238	29	1246	1629
<i>D3Bwg056</i>	10	115	82	293	435
<i>Kcnma1</i>	8	62	6	105	158
<i>Unc13a</i>	14	76	7	174	203
<i>Gm4392</i>	4	91	11	116	135
<i>Slc2a3</i>	14	24	4	66	78
<i>Sex6l</i>	11	34	9	44	110
<i>Cnrip1</i>	28	89	21	153	267
<i>Ccnd1</i>	90	9	13	158	129
<i>Khdrbs3</i>	64	128	30	128	325
<i>Ctnna2</i>	14	39	93	197	181
<i>Rab6b</i>	40	93	52	224	253
<i>Bend6</i>	27	20	12	91	78
<i>Necap1</i>	49	97	38	150	202
<i>Rufy3</i>	33	89	168	183	234
<i>Pgrmc1</i>	73	239	192	319	456
<i>Ptms</i>	136	206	83	338	430
<i>Gmfb</i>	76	152	186	294	398
<i>Myef2</i>	54	121	96	220	248
<i>Pea15a</i>	111	482	688	842	740
<i>Gnas</i>	90	223	186	392	419
<i>Hmgn1</i>	103	196	93	276	321
Microglia					
<i>P2ry12</i>	4666	25	92	9	4
<i>Tmem119</i>	2099	4	53	12	6
<i>Fcrls</i>	965	5	34	13	4
<i>Olfml3</i>	905	3	18	14	5
<i>Hexb</i>	8991	103	235	22	27
<i>Ctss</i>	4101	9	76	15	3
<i>Clqb</i>	3150	3	62	3	4
<i>Clqa</i>	2669	5	60	7	3
<i>Csf1r</i>	2905	4	80	24	7
<i>P2ry13</i>	1472	2	32	8	7
<i>Cx3cr1</i>	3836	6	79	21	7
<i>Gpr34</i>	838	1	16	13	1
<i>C1qc</i>	4558	8	109	15	8
<i>Mafb</i>	1382	5	14	18	11
<i>Tgfb1</i>	1678	27	75	22	25
<i>Fcgr1</i>	456	2	14	9	4
<i>Entpd1</i>	731	21	39	9	4
<i>Ltc4s</i>	461	4	28	5	3
<i>Csf3r</i>	294	2	5	12	6
<i>Il10ra</i>	604	3	15	25	5
<i>Egr1</i>	1968	163	12	63	58
<i>Siglech</i>	489	3	17	20	6
<i>Ccl2</i>	126	1	5	18	6
<i>Lag3</i>	246	8	11	8	2
<i>Fos</i>	1806	47	13	39	13

Supplementary Table 2:
Top unique microglial genes and shared genes between microglia, neurons, astrocytes and oligodendrocytes.

Top 40 Microglial unique genes	Microglia/Neuron genes	Microglia/Astrocyte genes	Microglia/Oligodendrocyte genes
<i>P2ry12</i>	<i>Asph</i>	<i>Sall1</i>	<i>C1qc</i>
<i>Tmem119</i>	<i>Basp1</i>	<i>Itgb5</i>	<i>C1qb</i>
<i>Olfml3</i>	<i>Cd34</i>	<i>Cst3</i>	<i>C1qa</i>
<i>P2ry13</i>	<i>Tanc2</i>	<i>Slc1a3</i>	<i>Ctss</i>
<i>Cx3cr1</i>	<i>Slc7a8</i>	<i>Gpr56</i>	<i>Timp2</i>
<i>Gpr34</i>	<i>Syng1</i>	<i>Mertk</i>	<i>Bin1</i>
<i>Hexb</i>	<i>Rgmb</i>	<i>Cables1</i>	<i>Frm4b</i>
<i>Rhob</i>	<i>Npnt</i>	<i>Sall3</i>	<i>Tmcc3</i>
<i>Jun</i>	<i>Mef2a</i>	<i>Etv5</i>	<i>Chn2</i>
<i>Rab3il1</i>	<i>Rtn4r1</i>	<i>Chst7</i>	<i>Gab1</i>
<i>Serpine2</i>	<i>Mef2c</i>	<i>Eya4</i>	<i>Spsb1</i>
<i>Ccl2</i>	<i>Khdrbs3</i>	<i>Arhgap5</i>	<i>Slc12a2</i>
<i>Scoc</i>	<i>Myo1b</i>	<i>Rnf180</i>	<i>Scarb2</i>
<i>Fcrls</i>	<i>Rtn1</i>	<i>Pmp22</i>	<i>Pdgfra</i>
<i>Siglech</i>		<i>Tmem144</i>	<i>Rap1gds1</i>
<i>Slc2a5</i>		<i>Npl</i>	<i>Pak1</i>
<i>Lrrc3</i>		<i>Trim47</i>	<i>Epn2</i>
<i>Plxdc2</i>		<i>Tir3</i>	
<i>Usp2</i>		<i>Itga6</i>	
<i>Ctsf</i>		<i>Abca1</i>	
<i>Cttnbp2nl</i>		<i>Tmem100</i>	
<i>Tgfb1</i>		<i>Arhgap12</i>	
<i>Atp8a2</i>		<i>Fads1</i>	
<i>Lgmn</i>		<i>Spire1</i>	
<i>Slco2b1</i>		<i>Tspan7</i>	
<i>Egr1</i>		<i>Jam2</i>	
<i>Mafb</i>		<i>Lrrc8a</i>	
<i>Bhlhe41</i>		<i>Il18</i>	
<i>Fcgr1a</i>			
<i>Ctsd</i>			
<i>Hpgds</i>			
<i>Hspa1a</i>			
<i>Adams1</i>			
<i>Lag3</i>			
<i>Csf1r</i>			
<i>F11r</i>			
<i>Golm1</i>			
<i>Nuak1</i>			
<i>Crybb1</i>			
<i>Ltc4s</i>			

Supplementary Table 2. Top unique microglial genes and shared genes between microglia and neurons, astrocytes and oligodendrocytes. The top 40 microglia specific genes are presented. Complete list of 152 microglia enriched genes are shown in [Source data – Supplementary Table 2](#).

**Supplementary Table 3:
Top microglia interactions by protein functions**

Object Type	Network Object name	Actual	Expected	Ratio	p-value
Transcription factors	PU.1	46	15.36	2.994	3.67E-11
	GCR-alpha	69	30.73	2.245	2.00E-10
	GATA-1	61	26.61	2.292	1.18E-09
	SP1	127	76.84	1.653	2.10E-09
	ETS2	28	7.537	3.715	2.88E-09
	HIF1A	47	19.03	2.469	1.19E-08
	CREB1	69	34.24	2.015	1.77E-08
	RelA (p65 NF-kB subunit)	59	27.55	2.141	2.70E-08
	NF-kB1 (p50)	35	12.35	2.835	3.54E-08
	MafB	15	2.572	5.832	4.33E-08
	C/EBPbeta	56	26.14	2.142	6.27E-08
	ETS1	48	20.89	2.298	7.57E-08
	SP3	35	12.79	2.736	8.49E-08
	c-Jun	54	25.38	2.127	1.38E-07
	BATF	11	1.454	7.567	1.88E-07
	STAT1	37	15.72	2.353	1.46E-06
	C/EBPalpha	44	20.84	2.111	2.64E-06
	p63	35	14.83	2.36	2.65E-06
	EIK-3	7	0.6486	10.79	2.73E-06
	PEA3	26	9.348	2.781	2.99E-06
Ligands	CCL8	7	0.5591	12.52	9.07E-07
	APOA1	11	2.55	4.314	5.05E-05
	TGF-beta 3	6	0.7157	8.384	6.70E-05
	Endostatin	7	1.096	6.388	1.02E-04
	TGF-beta 1	12	3.377	3.553	1.54E-04
	Cyr61	8	1.7	4.707	2.94E-04
	VIP	5	0.6486	7.709	4.17E-04
	LAMA2	3	0.1789	16.77	5.72E-04
	LIF	5	0.6933	7.212	5.75E-04
	SDF-1	7	1.543	4.536	8.73E-04
	CCL2	8	2.035	3.931	9.89E-04
	Galanin	4	0.4697	8.517	1.09E-03
	MIP-1-beta	5	0.8499	5.883	1.50E-03
	LAMC3	4	0.5144	7.776	1.56E-03
	LL37	5	0.9169	5.453	2.11E-03
	CCL13	5	0.9169	5.453	2.11E-03
	APOE	9	2.84	3.169	2.24E-03
	Fibrillin 1	7	1.879	3.726	2.75E-03
	FasL(TNFSF6)	9	2.93	3.072	2.77E-03
	IP10	6	1.431	4.192	3.04E-03
Receptors	Agtr1b	5	0.3131	15.97	9.28E-06
	Tissue factor	8	1.141	7.014	1.61E-05
	AGTR1	10	1.923	5.199	2.20E-05
	ITGB4	9	1.566	5.749	2.51E-05
	CXCR6	3	0.08946	33.54	4.37E-05
	CD9	10	2.192	4.563	6.87E-05
	BAMBI	5	0.492	10.16	1.05E-04
	TREM1	4	0.2907	13.76	1.50E-04
	CCR4	4	0.2907	13.76	1.50E-04
	ITGB1	16	5.613	2.85	1.81E-04
	Neuropilin-2	6	0.8946	6.707	2.44E-04
	VEGFR-2	12	3.578	3.354	2.64E-04
	EGFR	28	13.75	2.036	3.28E-04
	LDLR	7	1.364	5.131	4.11E-04
	ITGB8	4	0.3802	10.52	4.66E-04
	Endoglin	6	1.029	5.832	5.32E-04
	A2M receptor	13	4.428	2.936	5.40E-04
PTPRO	6	1.051	5.708	5.98E-04	
Plexin B1	5	0.738	6.775	7.75E-04	
TGF-beta receptor type III (betaglycan)	7	1.521	4.603	8.00E-04	
Enzymes	p300	40	21	1.905	7.76E-05
	JMJD3	14	4.182	3.348	8.49E-05
	MTCBP-1	3	0.1342	22.36	2.11E-04
	GCL cat	7	1.23	5.691	2.15E-04
	AOX1	5	0.5815	8.599	2.44E-04
	PLC-gamma 2	9	2.102	4.281	2.56E-04
	AK1BA	4	0.3355	11.92	2.77E-04
	GGT1	5	0.6038	8.28	2.94E-04
	FTase-alpha	5	0.6262	7.985	3.52E-04
	GNT-V	6	0.984	6.097	4.16E-04
	HPGD	4	0.4026	9.936	5.89E-04
	PLD2	7	1.476	4.742	6.67E-04
	PSAT	4	0.4249	9.413	7.33E-04
	NRHQR2	4	0.4249	9.413	7.33E-04
	TPST1	3	0.2013	14.9	8.44E-04
	TGM2	12	4.137	2.9	9.71E-04
	GAD1	5	0.8051	6.21	1.17E-03
	MAG1	3	0.2236	13.41	1.19E-03
	DPYD	4	0.492	8.13	1.31E-03
SYVN1	11	3.713	2.963	1.31E-03	
Kinases	p90RSK1	9	1.655	5.438	3.95E-05
	TSSK1	3	0.08946	33.54	4.37E-05
	JAK1	12	3.064	3.917	6.05E-05
	c-Src	29	13.49	2.15	1.02E-04
	FAK1	16	5.725	2.795	2.26E-04
	p38alpha (MAPK14)	17	6.396	2.658	2.63E-04
	VEGFR-2	12	3.578	3.354	2.64E-04
	EGFR	28	13.75	2.036	3.28E-04
	DYRK1a	9	2.281	3.945	4.72E-04
	p90RSK3(RPS6KA2)	5	0.738	6.775	7.75E-04
	TGF-beta receptor type III (betaglycan)	7	1.521	4.603	8.00E-04
	BMP receptor 2	8	2.013	3.975	9.20E-04
	Csk	12	4.249	2.824	1.22E-03
	PI3K cat class IA (p110-alpha)	8	2.214	3.613	1.71E-03
	TGF-beta receptor type II	10	3.355	2.981	2.06E-03
	KCRS	3	0.2684	11.18	2.10E-03
	MSK1	5	0.9393	5.323	2.36E-03
ErbB2	11	4.048	2.717	2.60E-03	

Supplementary Table 4:
Top microglial upstream regulators based on genearray profile identified by IPA™

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap
SMAD3	TR	Activated	3.569	6.74E-09
Ap1	complex	Activated	3.249	2.13E-07
SP1	TR	Activated	3.532	3.56E-07
EGR1	TR	Activated	2.479	4.06E-07
AR	ligand-dependent nuclear receptor	Activated	2.513	5.70E-06
ELK1	TR	Activated	2.357	6.50E-06
JUN	TR	Activated	2.39	9.42E-06
NFkB (complex)	complex	Activated	4.64	1.32E-05
EGR2	TR	Activated	2.94	1.76E-05
NFYA	TR	Activated	2.121	2.49E-05
NFKBIA	TR	Activated	2.824	2.63E-05
STAT4	TR	Activated	3.841	3.99E-05
NFATC2	TR	Activated	2.155	4.56E-05
MITF	TR	Activated	2.447	6.82E-05
ETS1	TR	Activated	2.918	8.05E-05
ARNT2	TR	Activated	3.742	1.05E-04
STAT3	TR	Activated	3.52	1.13E-04
RELA	TR	Activated	2.911	1.20E-04
SIM1	TR	Activated	3.742	1.42E-04
HIF1A	TR	Activated	2.389	1.61E-04
NFKB1	TR	Activated	2.615	1.65E-04
CEBPB	TR	Activated	2.315	2.18E-04
SMAD7	TR	Inhibited	-2.739	8.92E-07
KLF2	TR	Inhibited	-2.002	3.87E-06
IKZF1	TR	Inhibited	-3.162	6.22E-05
CBFB	TR	Inhibited	-2.121	1.00E-04
DACH1	TR	Inhibited	-2.2	1.16E-04
miR-29b-3p	mature microRNA	Inhibited	-2.183	8.12E-03
HOXA10	TR	Inhibited	-2.333	1.32E-02
miR-155-5p	mature microRNA	Inhibited	-2.789	1.33E-02
miR-16-5p	mature microRNA	Inhibited	-2.921	1.42E-02
miR-1	mature microRNA	Inhibited	-2.97	2.31E-02
MYC	TR	Inhibited	-2.28	2.76E-02
GFI1	TR	Inhibited	-2.236	3.22E-02

* TR, transcription regulator