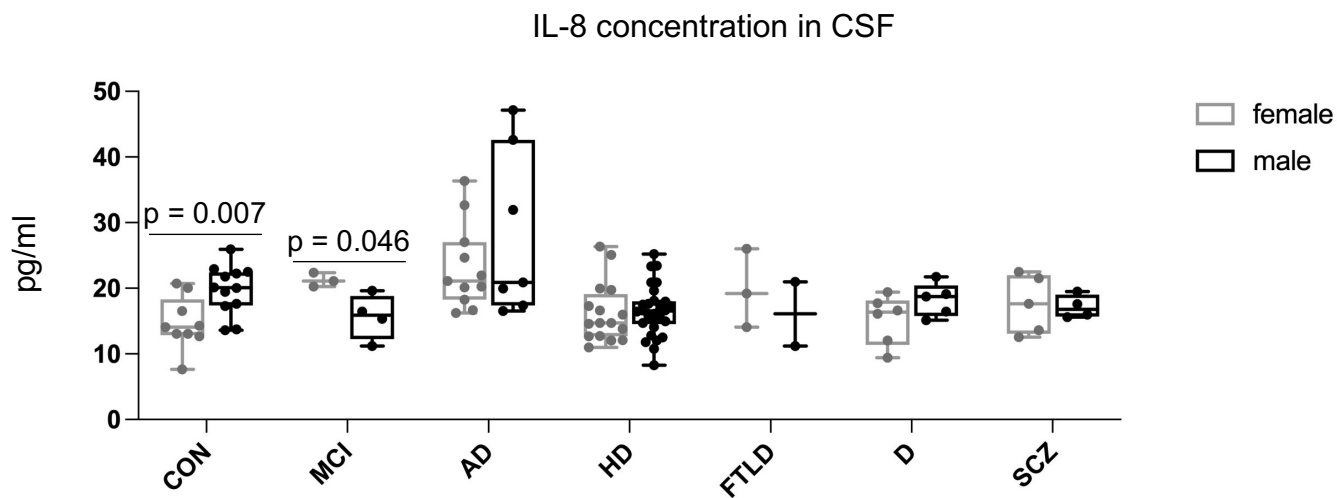
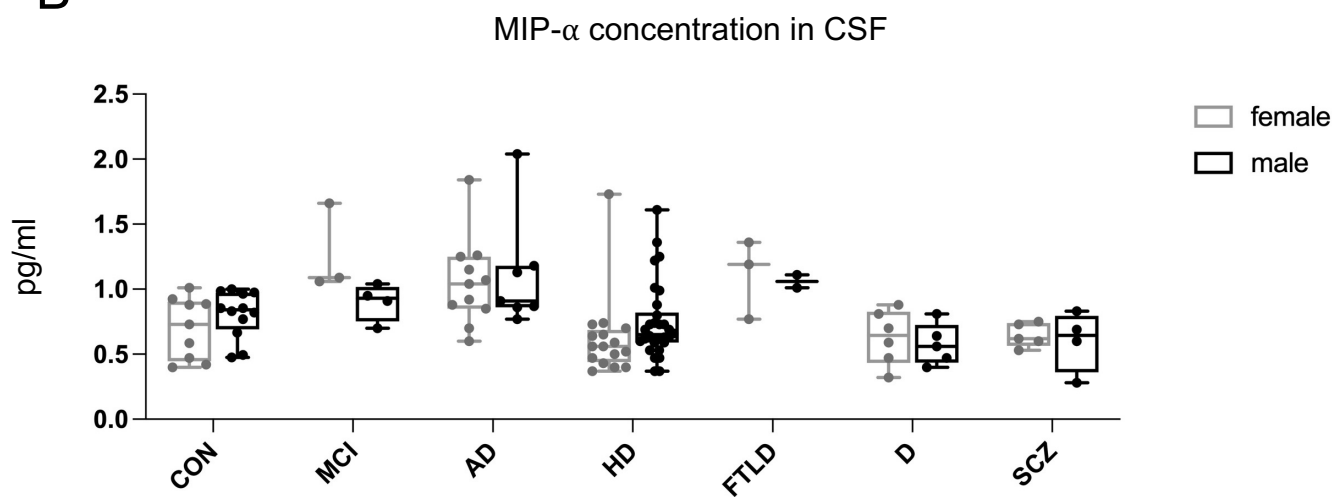


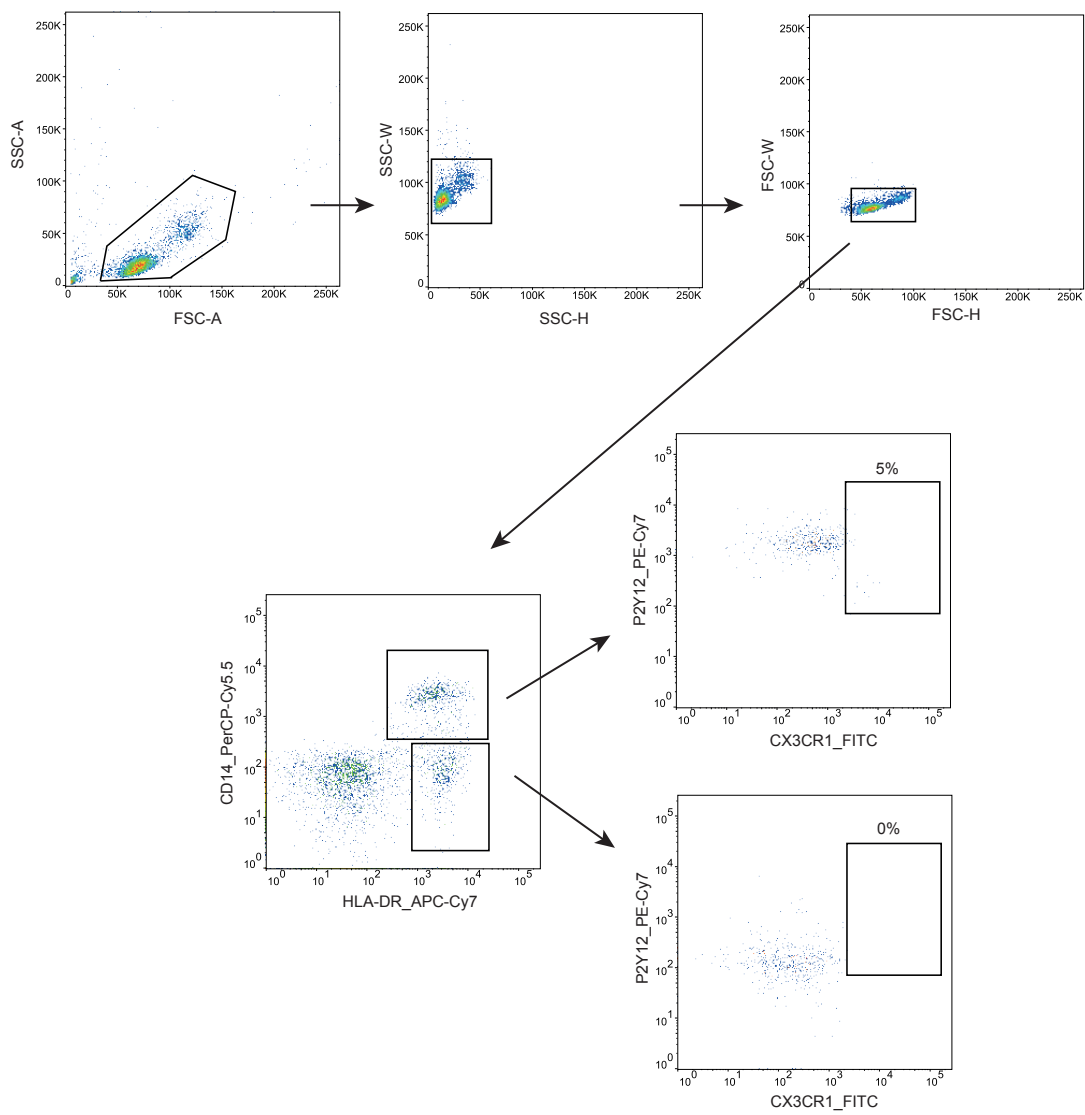
A



B



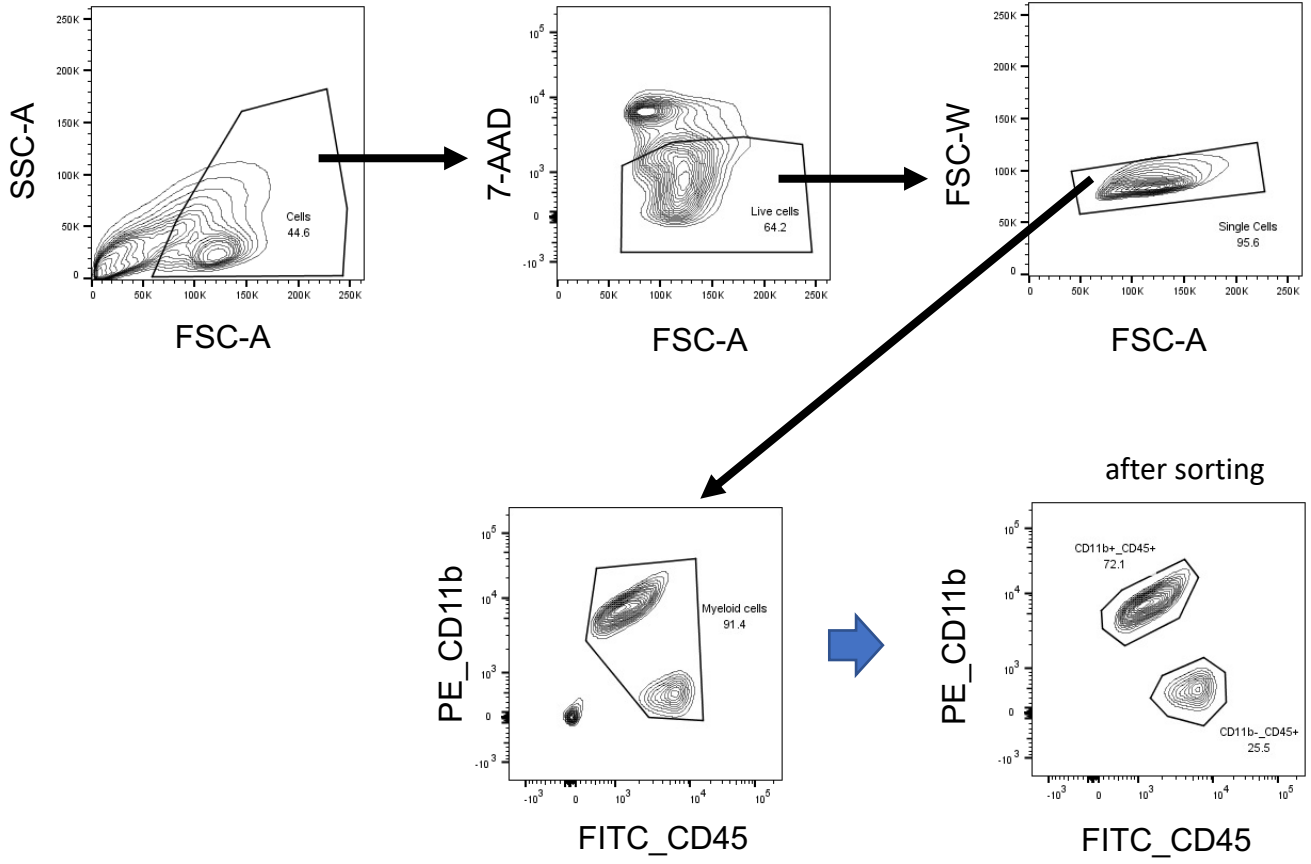
Supplementary Figure 3



Supplementary Figure 4

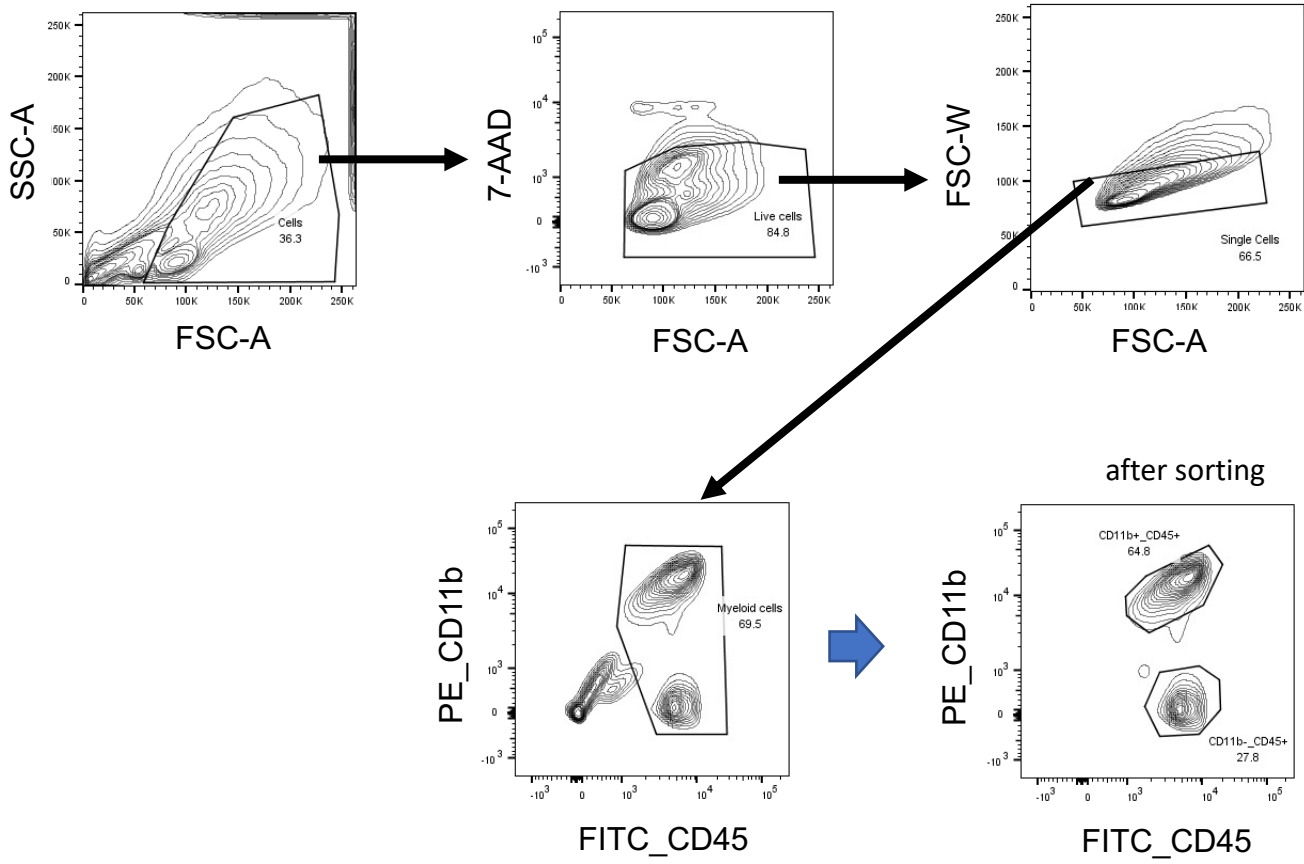
A

GFM



B

CP



Supplementary Figure 1 Gating strategy and cluster composition of PBMCs and CSF cells from *Panel 1*. **(A)** Gating strategy for CyTOF data prior to downstream analysis, selection of single CD45⁺ cells, debarcoding based on boolean gating of palladium barcodes and exclusion of CD3⁺CD19⁺ double positives. **(B)** UMAP plots with all cells per group, color coded by cluster ID for the 1-20 clusters obtained with the FlowSOM algorithm. **(C)** Cluster abundance per sample. **(D)** Median marker expression (with arcsinh transformation) for all lymphoids and myeloids, showing overall differences between PBMCs (n = 38, biological replication) and CSF cells (n = 28, biological replication). Boxes extend from the 25th to 75th percentiles. Whisker plots show the min (smallest) and max (largest) values. The line in the box denotes the median. Each dot represents the value of each sample.

Supplementary Figure 2 Phenotypic characterization of PBMCs and CSF cells using *Panel 2*. **(A)** MDS plot from all cells from CSF (pink) and peripheral blood (green), each dot represents a sample and dot size represents number of cells per sample. **(B)** NRS for each marker and all samples (PBMCs: n = 38, biological replication and CSF cells: n = 28, biological replication). Each dot represents the per-sample NR scores (colored by compartment ID). The empty black circles indicate the mean NR scores from all the samples. Boxes extend from the 25th to 75th percentiles. Whisker plots show the min (smallest) and max (largest) values. The line in the box denotes the median. The top ten markers were selected as embedding parameters for clustering analysis. **(C)** UMAP plots with all cells per group, color coded by cluster ID for the 1-20 clusters obtained with the FlowSOM algorithm. **(D)** Cluster abundance per sample, color coded by cluster ID, compartment identities are indicated in the bottom.

Supplementary Figure 3 The scatter plots show gender-related differences in IL-8 **(A)** and MIP-1 α **(B)** level in the CSF of CON individuals (9 females (F), 12 males (M), biological replication), or patients with MCI (3F, 4M), AD (11F, 7M), HD (16F, 30M), FTLD (3F, 2M), Depression (6F, 5M) or SCZ (5F, 4M). Boxes extend from the 25th to 75th percentiles. Whisker plots show the min (smallest) and max (largest) values. The line in the box denotes the median.

Each dot represents the value of each sample. Statistical significance was determined using unpaired, two-sided *t*-test.

Supplementary Figure 4 Gating strategy for FACS experiment in the **Figure 4E** and **4F**. P2Y₁₂⁺CXCR3⁺ cells were counted from the HLADR⁺CD14⁺ or HLADR⁺CD14⁻ populations as illustrated.

Supplementary Figure 5 Gating strategy for CD45⁺ CNS cells used in **Figure 7** and **8**. All CD45⁺ (CD11b⁺ and CD11b⁻) cells from GFM (**A**) and CP (**B**) were sorted using the same sorting strategy.

Supplementary Table 1. Donor and patients information

Related Figure	Group	CON	AD	MCI	HD	Depression	FTLD	SCZ
Fig. 1-6 (blood vs CSF)	n	21	18	7	46	11	5	9
	Female/Male	9/12	11/7	3/4	16/30	6/5	3/2	5/4
	Age, mean +/- SD (range, years)	62 +/- 14 (30-77)	72 +/- 10 (46-89)	78 +/- 1 (77-79)	49 +/- 11 (26-72)	57 +/- 19 (18-82)	62 +/- 4 (56-67)	46 +/- 19 (22-76)
	CyTOF (n)	11	8	7	12	-	-	-
	Luminex (n)	21	18	7	46	11	5	9
	Tau (pg/ml), mean +/- SD (range)	NA	597 +/- 453 (71-1584)	NA				
	pTau (pg/ml), mean +/- SD (range)		82,3 +/- 45,7 (29-167)					
	Aβ42 (pg/ml), mean +/- SD (range)		662 +/- 168 (409-1002)					
	Aβ40 (pg/ml), mean +/- SD (range)		15914 +/- 6228 (8421-27754)					
	Aβ42/40, mean +/- SD (range)		0,5 +/- 0,3 (0,06-0,92)					
Fig. 7 and 8 (CP vs GFM)	n	7	6	NA				
	Female/Male	4/3	2/4					
	Age, mean +/- SD (range, years)	55-103 (84 +/- 16)	82-98 (84 +/- 12)					
	CyTOF (n)	7	6					
	Luminex (n)	-	-					
	PMD, mean +/- SD (range, min)	461 +/- 88 (330-590)	326 +/- 63 (215-385)					
	CSF pH, mean +/- SD (range)	6.7 +/- 0.2 (6.39-6.89)	6.5 +/- 0.4 (5.94-6.92)					
	Braak Tau	2.8 +/- 1.2 (1-4)	5.7 +/- 0.5 (5-6)					
	Thal phase	2.2 +/- 1.7 (0-4)	4.7 +/- 0.5 (4-5)					

Supplementary Table 2. The *Panel 1* -antibody list (CSF vs peripheral blood, **Fig. 1**)

target	Isotope tag	clone	company	Dilution
surface				
CD19	¹⁴² Nd	HIB19	Fluidigm	1:100
HLA-DP	¹⁴³ Nd	Tü36	Biolegend	1:100
CD38	¹⁴⁴ Nd	HIT2	Fluidigm	1:100
CD4	¹⁴⁵ Nd	RPA-T4	Fluidigm	1:100
CD11c	¹⁴⁷ Sm	Bu15	Fluidigm	1:100
CD16	¹⁴⁸ Nd	3G8	Fluidigm	1:50
CD37	¹⁵⁰ Nd	M-B371	Biolegend	1:100
CD35	¹⁵¹ Eu	594708	R&D	1:100
CD66b	¹⁵² Sm	80H3	Fluidigm	1:400
CD3	¹⁵⁴ Sm	UCHT1	Fluidigm	1:200
CD56	¹⁵⁵ Gd	NCAM16.2	Fluidigm	1:100
CCR5	¹⁵⁶ Gd	NP6G4	Fluidigm	1:100
CD369	¹⁵⁸ Gd	15E2	Biolegend	1:100
CD14	¹⁶⁰ Dy	RM052	Fluidigm	1:200
EMR1	¹⁶¹ Dy	A10	Bio-Rad	1:100
CD8a	¹⁶² Dy	RPA-T8	Fluidigm	1:100
CXCR3	¹⁶³ Dy	G025H7	Fluidigm	1:300
CD115	¹⁶⁴ Dy	9-4D2-1E4	Biolegend	1:50
CD74	¹⁶⁶ Er	LN2	Fluidigm	1:100
CD130	¹⁶⁸ Er	2E1B02	Fluidigm	1:100
CD33	¹⁶⁹ Tm	WM53	Fluidigm	1:100
GPR56	¹⁷⁰ Er	CG4	Biolegend	1:50
TREM2	¹⁷¹ Yb	KBZ0318011	R&D	1:50
CX3CR1	¹⁷² Yb	2A9-1	Fluidigm	1:50
CD141	¹⁷³ Yb	1A4	Fluidigm	1:100
CD61	^{Bi209} Di	VI-PL2	Fluidigm	1:100
intracellular				
TNF	¹⁴⁶ Nd	MAb11	Biolegend	1:100
CCL2	¹⁴⁹ Sm	5D3-F7	Biolegend	1:200
IL6	¹⁵³ Eu	MQ2-13A5	Biolegend	1:100
IRF4	¹⁵⁹ Tb	IRF4.3E4	Biolegend	1:100
IRF8	¹⁶⁵ Ho	7G11A45	Biolegend	1:100
ABCA7	¹⁶⁷ Er	polyclonal	Merck	1:50
C3	¹⁷⁴ Yb	4C6A8	Novus Biologicals	1:50
APOE	¹⁷⁵ Lu	WUE-4	Novus Biologicals	1:100
MRP14-APC	-	MRP 1H9	Biolegend	1:200
APC	¹⁷⁶ Yb	APC003	Fluidigm	1:100

Supplementary Table 3. The *Panel 2*-antibody list (CSF vs peripheral blood, **Fig. 2**)

target	Isotope tag	clone	company	Dilution
surface				
HLA-DR	¹⁴¹ Pr	L243	Biolegend	1:100
CD116	¹⁴² Nd	4H1	Fluidigm	1:100
CD11b	¹⁴⁴ Nd	ICRF44	Fluidigm	1:100
CD4	¹⁴⁵ Nd	RPA-T4	Fluidigm	1:100
CD64	¹⁴⁶ Nd	10.1	Fluidigm	1:50
CD11c	¹⁴⁷ Sm	3.9	Fluidigm	1:100
CD56	¹⁴⁹ Sm	NCAM16.2	Fluidigm	1:100
CD95	¹⁵² Sm	DX2	Fluidigm	1:100
TIM3	¹⁵³ Eu	F38-2E2	Miltenyi	1:100
CD172a	¹⁵⁴ Sm	15-414	Biolegend	1:100
CD54 (ICAM1)	¹⁵⁵ Gd	HA58	Biolegend	1:100
CD274 (PD-L1)	¹⁵⁶ Gd	29E.2A3	Fluidigm	1:100
CD169	¹⁵⁸ Gd	7-239	Fluidigm	1:100
CD163	¹⁶⁰ Dy	GHI/61	Fluidigm	1:50
TIM4	¹⁶¹ Dy	9F4	Fluidigm	1:50
CD91	¹⁶² Dy	A2MR- α 2	BD Bioscience	1:100
Galectin9	¹⁶³ Dy	9M1-3	Fluidigm	1:100
TMEM119	¹⁶⁴ Dy	A16075D	Biolegend	1:50
CD16	¹⁶⁵ Ho	3G8	Fluidigm	1:50
CD44	¹⁶⁶ Er	BJ18	Fluidigm	1:100
MS4A4A	¹⁶⁷ Er	818112	R&D Systems	1:50
CD206	¹⁶⁸ Er	15-2	Biolegend	1:50
TGF- β	¹⁶⁹ Tm	TW4-2F8	Biolegend	1:50
P2Y12 (biotin)	-	polyclonal	Sigma-Aldrich	1:200
Biotin	¹⁷⁰ Er	1D4-C5	Fluidigm	1:100
CCR2	¹⁷¹ Yb	K036C2	Biolegend	1:100
CLEC12A	¹⁷³ Yb	50C1	Fluidigm	1:100
AXL	¹⁷⁵ Lu	polyclonal	LSBio	1:50
CD47	^{Bi209} Di	CC2C6	Fluidigm	1:200
intracellular				
NFAT1	¹⁴³ Nd	D43B1	Fluidigm	1:100
Galanin	¹⁴⁸ Nd	581403	Fluidigm	1:100
MIP-1 β (CCL4)	¹⁵⁰ Nd	D211351	Fluidigm	1:200
CD68	¹⁵¹ Eu	Y1/82A	Biolegend	1:100
IL-1 β	¹⁷⁴ Yb	CRM56	eBioscience	1:100
OPN	¹⁷² Yb	polyclonal	LSBio	1:50
IFN α -APC	-	LT27:295	Miltenyi Biotec	1:100
APC	¹⁷⁶ Yb	APC003	Fluidigm	1:100

Supplementary Table 4. The list of antibodies used for *ex vivo* experiment (Fig. 5)

target clone	Isotope tag	clone	company	dilution
surface				
CD45	89Y	HI30	Fluidigm	1:200
HLA-DR	141Pr	L243	Biolegend	1:100
CD19	142Nd	HIB19	Fluidigm	1:100
CD38	144Nd	HIT2	Fluidigm	1:100
CD4	145Nd	RPA-T4	Fluidigm	1:100
CD64	146Nd	10.1	Fluidigm	1:50
CD11c	147Sm	Bu15	Fluidigm	1:100
CD16	148Nd	3G8	Fluidigm	1:50
CD56	149Sm	NCAM16.2	Fluidigm	1:100
CD35	151Eu	594708	R&D	1:100
CD95	152Sm	DX2	Fluidigm	1:100
CD3	154Sm	UCHT1	Fluidigm	1:200
CCR5	156Gd	NP6G4	Fluidigm	1:100
CD14	160Gd	RM052	Fluidigm	1:200
CD36	161Dy	5-271	Biolegend	1:100
CD8	162Dy	RPA-T8	Fluidigm	1:100
CXCR3	163Dy	G025H7	Fluidigm	1:300
CD115	164Dy	9-4D2-1E4	Biolegend	1:50
P2Y12-biotin	-	polyclonal	Sigma-Aldrich	1:200
Biotin	165Ho	1D4-C5	Biolegend	1:100
CD141	166Er	M80	Fluidigm	1:100
CD33	169Tm	WM53	Fluidigm	1:100
GPR56	170Er	CG4	Biolegend	1:50
CCR2	171Yb	K036C2	Biolegend	1:100
Clec12A	173Yb	50C1	Fluidigm	1:100
CCR6	176Yb	11A9	Fluidigm	1:200
CD11b	209Bi	ICRF44	Fluidigm	1:200
Intracellular				
cPARP	143Nd	F21-852	Fluidigm	1:100
MIP-1 β (CCL4)	150Nd	D211351	Fluidigm	1:200
CD68	153Eu	Y1/82A	Biolegend	1:100
IL-10	158Gd	JES3-9D7	Biolegend	1:100
IRF4	159Tb	IRF4.3E4	Biolegend	1:100
IRF8	167Er	7G11A45	Biolegend	1:100
IFN γ	168Er	B27	Fluidigm	1:100
IL-6	167Er	MQ2-13A5	Biolegend	1:100
OPN	172Yb	polyclonal	LSBio	1:50
IL-8-FITC	-	BH0814	Biolegend	1:200
FITC	174Yb	FIT-22	Fluidigm	1:100
TNF	175Lu	Mab11	Fluidigm	1:100

Supplementary Table 5. The list of antibodies used for *ex vivo* experiment (Fig. 6)

target clone	Isotope tag	clone	company	Dilution
surface				
CD45	89Y	HI30	Fluidigm	1:200
P2Y12-biotin	-	polyclonal	Sigma-Aldrich	1:200
Biotin	111Cd	1D4-C5	Biolegend	1:200
CD49d	141Pr	9F10	Fluidigm	1:100
CD19	142Nd	HIB19	Fluidigm	1:100
HLA-DR	143Nd	L243	Fluidigm	1:100
CD69	144Nd	FN50	Fluidigm	1:100
CD4	145Nd	RPA-T4	Fluidigm	1:100
CD64	146Nd	10.1	Fluidigm	1:50
CD123	147Sm	6H6	Biolegend	1:100
CD16	148Nd	3G8	Fluidigm	1:50
CD56	149Sm	NCAM16.2	Fluidigm	1:100
MERTK	151Eu	125518	R&D System	1:100
CD66b	152Sm	80H3	Fluidigm	1:400
CD3	154Sm	UCHT1	Fluidigm	1:200
CD11c	155Gd	44807	Fluidigm	1:100
CD61	156Gd	VI-PL2	Biolegend	1:100
CD1c	159Tb	L161	Biolegend	1:100
CD14	160Gd	RM052	Fluidigm	1:200
CD163	163Dy	GHI/61/Fluidigm	Fluidigm	1:50
CD115	164Dy	9-4D2-1E4	Biolegend	1:50
TGF- β (LAP)	166Er	TW4-2F8	Biolegend	1:50
CD206	168Er	15-2	Fluidigm	1:50
CCR2	169Tm	K036C2	Fluidigm	1:100
GPR56	170Er	CG4	Biolegend	1:50
TREM2	171Yb	237920	R&D System	1:50
CX3CR1	172Yb	2A9-1	Fluidigm	1:50
CXCR4	173Yb	12G5	Fluidigm	1:200
CCR6	176Yb	11A9	Fluidigm	1:200
CD11b	209Bi	ICRF44	Fluidigm	1:200
Intracellular				
CXCL12-FITC	-	79018	Thermofisher	1:50
FITC	114Cd	FIT-22	Biolegend	1:200
CXCL10-PE	-	4NY8UN	eBioscience™	1:50
PE	116Cd	PE001	Biolegend	1:200
MIP-1 β (CCL4)	150Nd	D211351	Fluidigm	1:200
CD68	153Eu	Y1/82A	Biolegend	1:100
IL-10	158Gd	JES3-9D7	Biolegend	1:100
CTLA-4	161Dy	14D3	Fluidigm	1:100
TNF	162Dy	MAB11	Biolegend	1:100
IFN γ	165Ho	B27	Fluidigm	1:100
IL-6	167Er	MQ2-13A5	Biolegend	1:100
IL-1 β	174Yb	CRM56	Invitrogen	1:100
ApoE	175Lu	WUE-4	Novus Biologicals	1:100

Supplementary Table 6. The list of antibodies used for an differential analysis of immune cells in CP and GFM - *Panel A* (Fig. 7)

target clone	isotope tag	clone	company	dilution
surface				
CD19	¹⁴² Nd	HIB19	Fluidigm	1:100
HLA-DR	¹⁴³ Nd	L243	Fluidigm	1:100
CD44	¹⁴⁴ Nd	BJ18	Biolegend	1:50
CD4	¹⁴⁵ Nd	RPA-T4	Fluidigm	1:100
CD11c	¹⁴⁷ Sm	Bu15	Fluidigm	1:100
CD16	¹⁴⁸ Nd	3G8	Fluidigm	1:50
CD86	¹⁵⁰ Nd	IT2.2	Fluidigm	1:100
CD35	¹⁵¹ Eu	594708	R&D Systems	1:100
CD83	¹⁵² Sm	HB15e	Biolegend	1:100
CD3	¹⁵⁴ Sm	UCHT1	Fluidigm	1:200
CD56	¹⁵⁵ Gd	NCAM16.2	Fluidigm	1:100
CCR5	¹⁵⁶ Gd	NP6G4	Fluidigm	1:100
CD169	¹⁵⁸ Gd	7-239	Fluidigm	1:100
CD22	¹⁵⁹ Tb	HIB22	Fluidigm	1:100
CD14	¹⁶⁰ Dy	RMO52	Fluidigm	1:200
EMR1	¹⁶¹ Dy	A10	Bio-Rad	1:100
CD8a	¹⁶² Dy	RPA-T8	Fluidigm	1:100
CXCR3	¹⁶³ Dy	G025H7	Fluidigm	1:300
CD115	¹⁶⁴ Dy	9-4D2-1E4	Biolegend	1:50
CD74	¹⁶⁶ Er	LN2	Fluidigm	1:100
CD130	¹⁶⁸ Er	2E1B02	Fluidigm	1:100
TGF-β	¹⁶⁹ Tm	TW4-2F8	Biolegend	1:50
GPR56	¹⁷⁰ Er	CG4	Biolegend	1:50
CXCR5	¹⁷¹ Yb	RF8B2	Fluidigm	1:100
CX3CR1	¹⁷² Yb	2A9-1	Biolegend	1:50
CD141	¹⁷³ Yb	1A4	Fluidigm	1:100
AXL	¹⁷⁵ Lu	polyclonal	LSBio	1:50
CD61	^{Bi209} Di	VI-PL2	Fluidigm	1:100
intracellular				
TNF	¹⁴⁶ Nd	MAb11	Fluidigm	1:100
CCL2	¹⁴⁹ Sm	5D3-F7	Biolegend	1:200
IL-6	¹⁵³ Eu	MQ2-13A5	Biolegend	1:100
IRF8	¹⁶⁵ Ho	7G11A45	Biolegend	1:100
ABCA7	¹⁶⁷ Er	polyclonal	Merck	1:50
C3	¹⁷⁴ Yb	4C6A8	Novus Biologicals	1:50
MRP14-APC	-	MRP 1H9	Biolegend	1:200
APC	¹⁷⁶ Yb	APC003	Fluidigm	1:100

Supplementary Table 7. The list of antibodies used for an differential analysis of immune cells in CP and GFM - *Panel B* (Fig. 8)

target clone	Isotope tag	clone	company	dilution
surface				
HLA-ABC	¹⁴¹ Pr	W6/36	Fluidigm	1:200
CD116	¹⁴² Nd	4H1	Fluidigm	1:100
CD11b	¹⁴⁴ Nd	ICRF44	Fluidigm	1:100
CD18	¹⁴⁵ Nd	TS1/18	Biolegend	1:100
CD64	¹⁴⁶ Nd	10.1	Fluidigm	1:50
CD11c	¹⁴⁷ Sm	3.9	Fluidigm	1:100
CD14	¹⁴⁸ Nd	RM052	Fluidigm	1:100
CD95	¹⁵² Sm	DX2	Fluidigm	1:100
TIM3	¹⁵³ Eu	F38-2E2	Miltenyi Biotec	1:100
CD172a	¹⁵⁴ Sm	15-414	Biolegend	1:100
CD54	¹⁵⁵ Gd	HA58	Biolegend	1:100
PDL1	¹⁵⁶ Gd	29E.2A3	Fluidigm	1:100
CD369	¹⁵⁸ Gd	15E2	Biolegend	1:100
CD163	¹⁶⁰ Dy	GHI/61	Fluidigm	1:100
CD36	¹⁶¹ Dy	5-271	Biolegend	1:100
CD91	¹⁶² Dy	A2MR- α 2	BD Bioscience	1:100
GLUT 5	¹⁶³ Dy	195205	R&D Systems	1:100
TMEM119	¹⁶⁴ Dy	A16075D	Biolegend	1:50
CD32-PE	-	6C4(CD32)	eBioscience	1:100
PE	¹⁶⁵ Ho	PE001	Fluidigm	1:100
MS4A4A	¹⁶⁷ Er	818112	R&D Systems	1:50
CD206	¹⁶⁸ Er	15-2	Biolegend	1:50
CD33	¹⁶⁹ Tm	WM53	Fluidigm	1:100
P2Y12 (biotin)	-	polyclonal	Sigma-Aldrich	1:200
Biotin	¹⁷⁰ Er	1D4-C5	Fluidigm	1:100
TREM2	¹⁷¹ Yb	KBZ0318011	R&D	1:50
CD9	¹⁷² Yb	SN4 C3-3A2	Fluidigm	1:100
CLEC12A	¹⁷³ Yb	50C1	Fluidigm	1:100
CD47	^{Bi209} Di	CC2C6	Fluidigm	1:200
intracellular				
IKZF1	¹⁴³ Nd	16B5C71	Fluidigm	1:100
MIP-1 β (CCL4)	¹⁵⁰ Nd	D211351	Fluidigm	1:200
CD68	¹⁵¹ Eu	Y1/82A	Biolegend	1:100
GMCSF	¹⁵⁹ Tb	BVD2-21C11	Biolegend	1:100
IL-10	¹⁶⁶ Er	JES3-9D7	Biolegend	1:100
IL-1 β	¹⁷⁴ Yb	CRM56	eBioscience	1:100
APOe	¹⁷⁵ Lu	polyclonal	LSBio	1:100
IFN α -APC	-	LT27:295	Miltenyi Biotec	1:100
APC	¹⁷⁶ Yb	APC003	Fluidigm	1:100