

**Supplementary Table1. The list of antibodies for CyTOF.**

Antibodies	Source	Identifier
anti-mouse CCR2, 156Gd, monoclonal	R&D	Cat# MAB55381-100; RRID:AB_2749828
anti-mouse CD45, 89Y, monoclonal	FDM	Cat# 3089005B; RRID:AB_2651152
anti-mouse CD11c, 209Bi, monoclonal	FDM	Cat# 3142003B; RRID:AB_2814737
anti-mouse CD11b, 148Nd, monoclonal	FDM	Cat# 3143015B; RRID:AB_2811240
anti-mouse I-A/I-E, 150Nd, monoclonal	Biolegend	Cat# 107637; RRID:AB_2563771
anti-mouse CD86, 151Eu, monoclonal	Biolegend	Cat# 105001; RRID:AB_313144
anti-mouse MERTK, 153Eu, monoclonal	R&D	Cat# MAB5912-100 RRID:AB_2832245
anti-mouse F4/80, 146Nd, monoclonal	FDM	Cat# 3159009B; RRID:AB_2811238
anti-mouse CD64, 160Gd, monoclonal	R&D	Cat# MAB20741; RRID:AB_2246880
anti-mouse Ly6G, 161Dy, monoclonal	Biolegend	Cat# 127637; RRID:AB_2563784
anti-mouse SiglecH, 163Dy, monoclonal	Biolegend	Cat# 129602; RRID:AB_1227757
anti-mouse CX3CR1, 164Dy, monoclonal	FDM	Cat# 3164023B; RRID:AB_2832247
anti-mouse CD206 (MMR), 169Tm, monoclonal	FDM	Cat# 3169021B; RRID:AB_2832249
anti-mouse CD169, 171 Yb, monoclonal	Biolegend	Cat# 142404; RRID:AB_10915697
anti-mouse Ly6C, 111Cd, monoclonal	Biolegend	Cat# 128039; RRID:AB_2563783
anti-mouse Iba1, 158Gd, monoclonal	Abcam	Cat# ab178846; RRID:AB_2636859
anti-mouse BDNF, 112 Cd, monoclonal	Abcam	Cat# ab216443; RRID:AB_2892087
anti-mouse TGF $\beta$ , 159Tb, monoclonal	Biolegend	Cat# 141402; RRID:AB_10719836
anti-mouse pNFkb, 142Nd, monoclonal	Biolegend	Cat# 653002; RRID:AB_2561613
anti-mouse IL-1a, 147Sm, monoclonal	Biolegend	Cat# 503206; RRID:AB_315284
anti-mouse MCP1, 166Er, monoclonal	Thermo Fisher Scientific	Cat# MA5-17040; RRID:AB_2538512

**Supplementary Table2. A list of the 10 human TREM2 interacting proteins with highest intensity.**

	<b>Gene Symbol</b>	<b>Protein</b>	<b>UniProt Accession</b>
1.	TMPO	Lamina-associated polypeptide 2, isoform alpha	P42166
2.	LIG3	DNA ligase 3	P49916
3.	BANF1	Barrier-to-autointegration factor	O75531
4.	XRCC1	DNA repair protein XRCC1	P18887
5.	SUPT16H	FACT complex subunit SPT16	Q9Y5B9
6.	HIST2H3PS2	Histone H3	Q5TEC6
7.	ACTA1; ACTC1; ACTA2; ACTG2	Actin, alpha skeletal muscle; Actin, alpha cardiac muscle 1; Actin, aortic smooth muscle; Actin, gamma-enteric smooth muscle	P68133; P68032; P62736; P63267
8.	CTSF	Cathepsin F	Q9UBX1
9.	HELZ	Probable helicase with zinc finger domain	P42694
10.	H2AFY	Core histone macro-H2A.1	O75367

**Supplementary Table3. Basic characteristics of human tissue donors.**

Mayo ID	TDP-43	Thal phase	Duration(year)	Age	Sex
ALS1	1	3	5	53	F
ALS2	1	0	2	60	M
ALS3	1	0	2	59	F
ALS4	1	0	3	58	F
ALS5	1	0	5	60	F
ALS6	1	0	7	64	M
ALS7	1	0	1	72	F
ALS8	1	1	3	65	F
ALS9	1	1	4	62	F
ALS10	1	4	3	60	F
ALS11	1	0	NA	64	F
ALS12	1	2	NA	75	M
ALS13	1	3	NA	78	M
ALS14	1	2	NA	79	F
ALS15	1	1	NA	80	M
ALS16	1	3	NA	83	F
Control 1	0	0	NA	64	M
Control 2	0	3	NA	75	M
Control 3	0	3	NA	85	M
Control 4	0	0	NA	77	M
Control 5	0	0	NA	92	F
Control 6	0	0	NA	83	F
Control 7	0	0	NA	67	M
Control 8	0	0	NA	79	F
Control 9	0	0	NA	80	F
Control 10	0	0	NA	54	F
Control 11	0	0	NA	76	M
Control 12	1	0	NA	64	F

ALS: amyotrophic lateral sclerosis