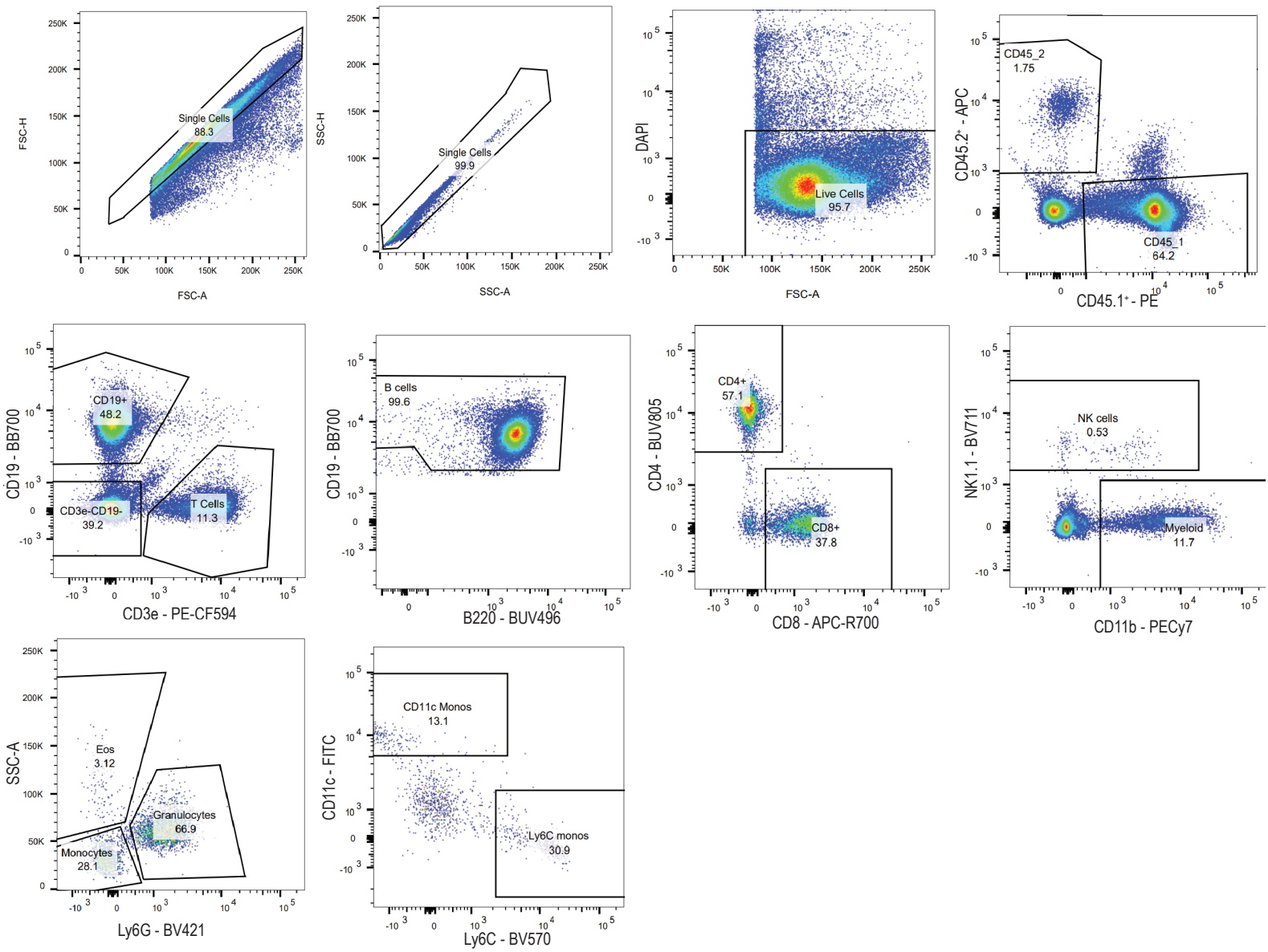
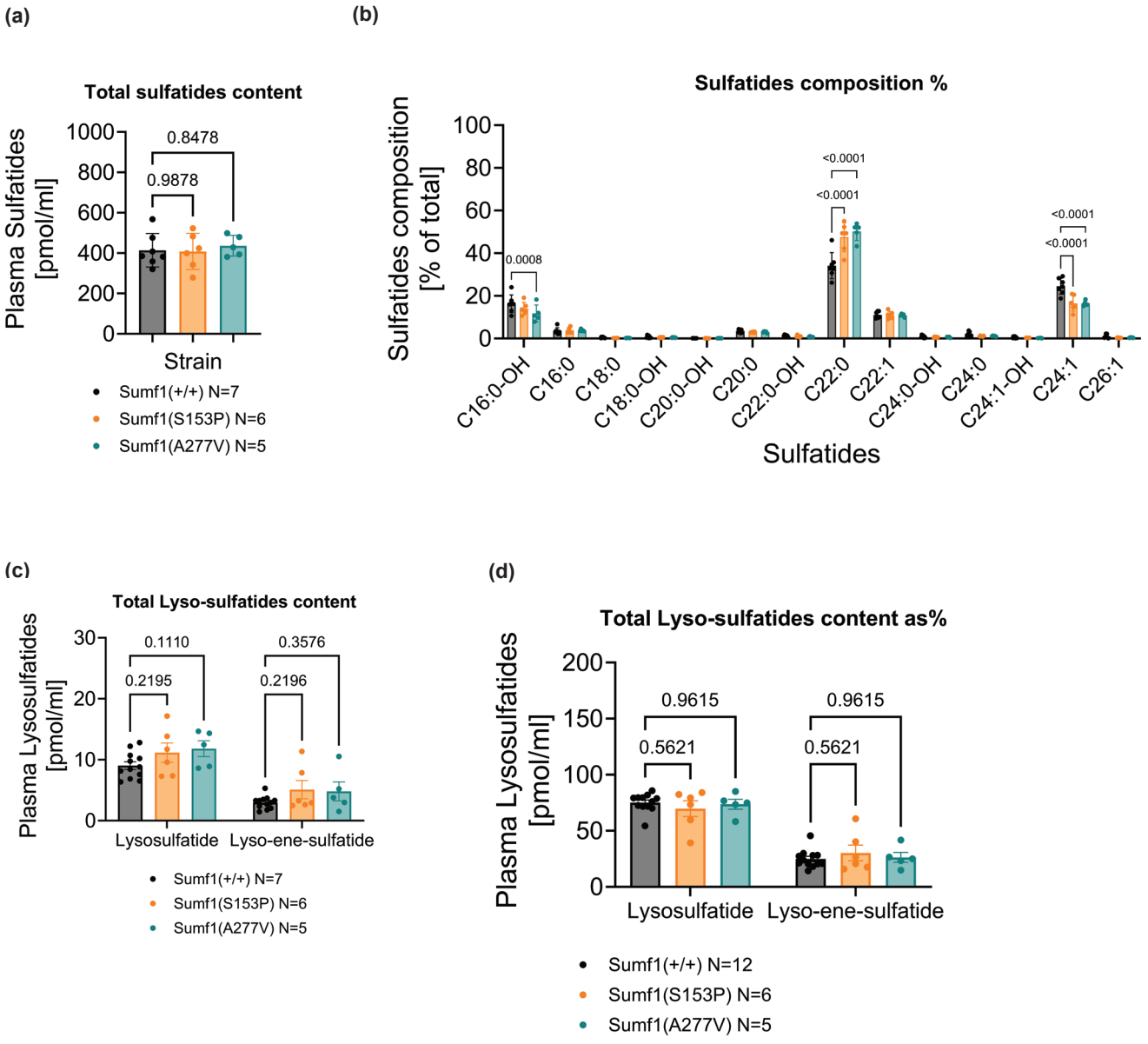


Supplementary Figure 1a: Flow cytometry gating strategy for spleen analysis

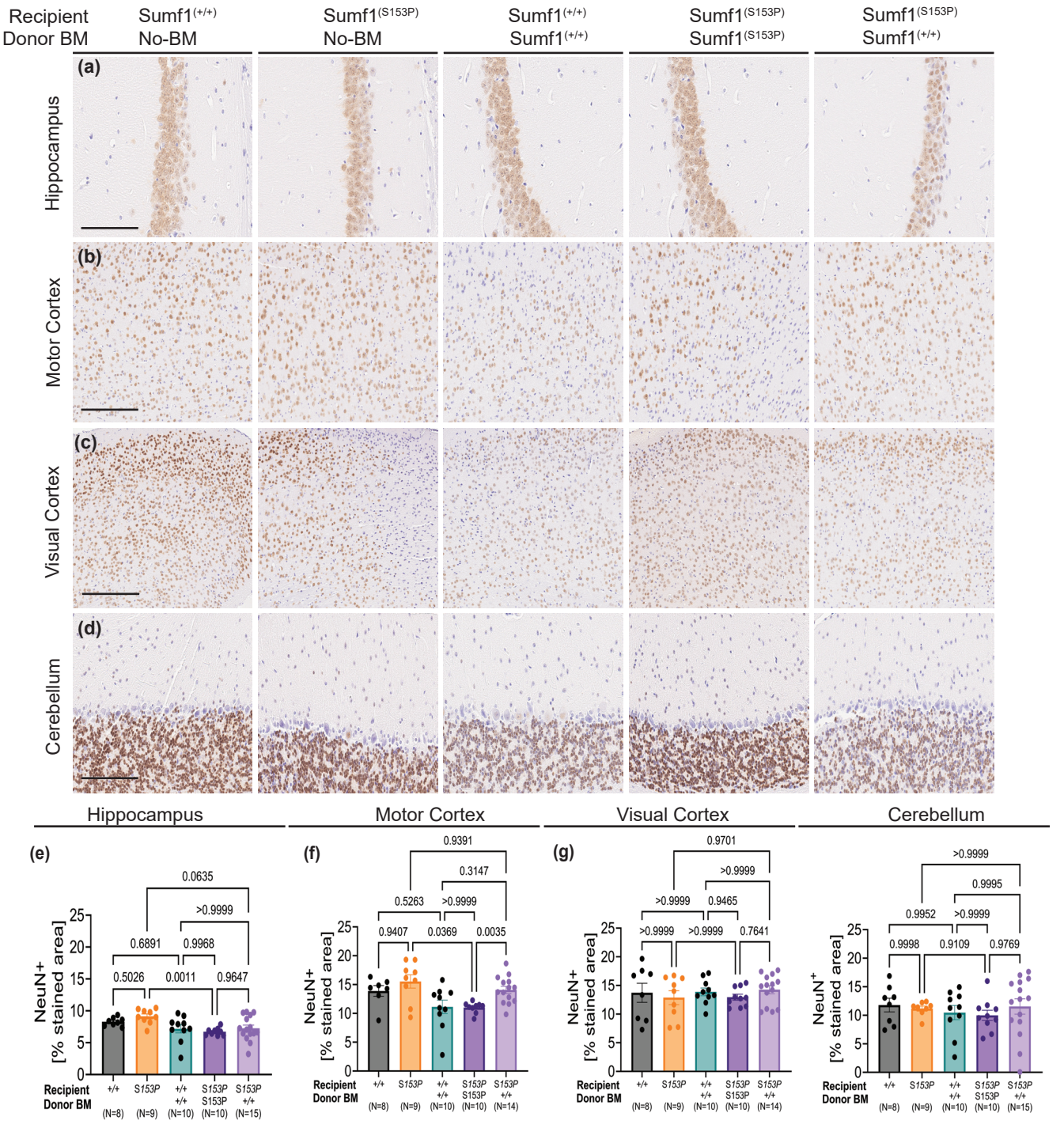
Representative gating strategy for B-cells, T-cells, T-CD4 and T-CD8 as measured by flow cytometry. First, doublet discrimination is performed with a double gate (FSC-H/FSC-A ans SSC-H/SSC-A). Only viable cells are evaluated, identified by low DAPI and FSC-A.
From the live cells population gate, the two CD45+ population (resident and transplanted cells) are identified with CD45.2$^+$/CD45.1$^+$. Total T-Cells population was defined as CD19$^-$ CD3e$^+$. The B-Cells are identified throught the CD19/B220 from CD19$^+$ cells. While CD4$^+$ and CD8$^+$ population are gated from T-cells population using CD4/CD8.
To analyze the eosinophil (Eos), monocytes and the granulocytes populations, the gate strategy to select the myeloid cells is applied using NK1.1/CD11b from CD3e-CD19-. Finaly the CD11c monocytes are gated from the myeloid population.

Supplementary Table 1: Antibodies used for flow cytometry analysis.

Fluorochrome	Marker	Catalog#	Company	Clone
FITC	CD11c	35-0114-U100	Tonbo	N418
BB700	CD19	566411	BD Biosciences	1D3
PE	CD45.1	110708	BioLegend	A201.7
PE-CF594	CD3e	562286	BD Biosciences	145-2C11
PC7	CD11b	552850	BD Biosciences	M1/70
APC	CD45.2	20-0454-u100	Tonbo	1042.1
APC-R700	CD8	564983	BD Biosciences	53-6.72
BV421	Ly6G	562737	BD Biosciences	1A8
BV570	Ly6C	128029	BioLegend	HK1.4
BV711	NK1.1	108745	BioLegend	PK136
BUV496	B220	612950	BD Biosciences	RA3-6B2
BUV805	CD4	564922	BD Biosciences	GK1.5
DAPI	N/A	N/A	N/A	N/A

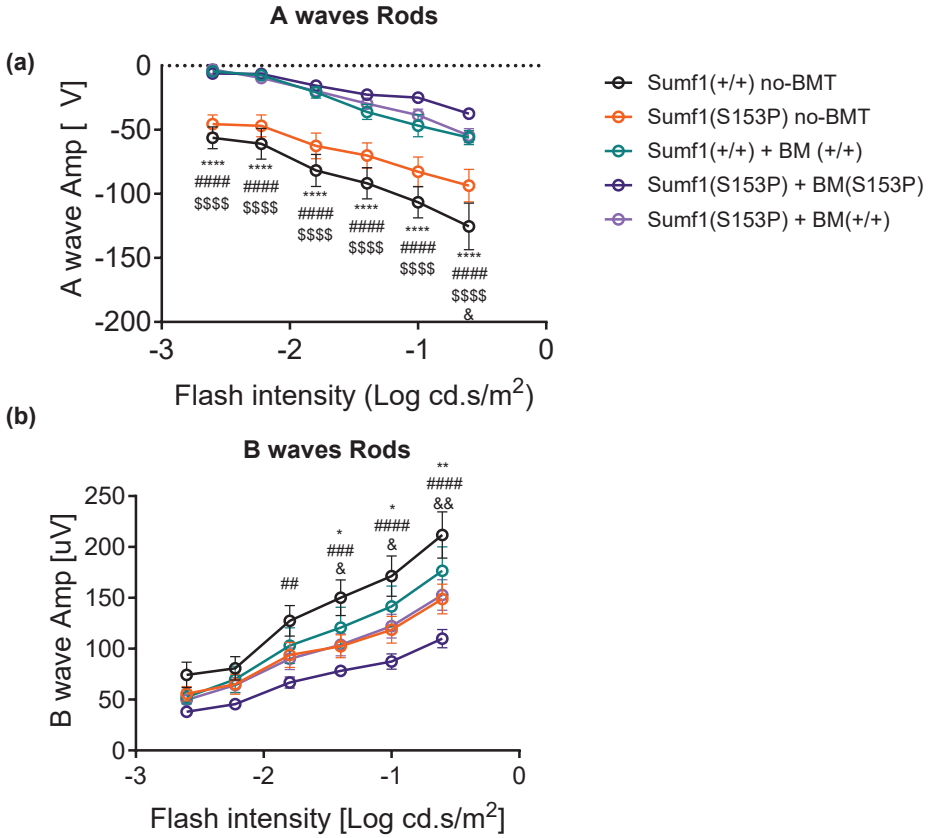


Supplementary Figure 2: Sulfatides and Lyso-sulfatides content in Sumf1 mutant mice.
Sulfatides and Lyso-sulfatides were assessed in plasma samples of Sum1(S153P) and Sumf1(A277V) homozygous mice at 6 months of age. **a** Total sulfatide content. **b** Composition of different sulfatides species as percentage of total. **c** Lyso-sulfatides content represented as concentration or **d** percentage of total. Bar graphs represent the mean ± SD, N = 5-12, mixed sex. Statistical significance was assessed by two-way ANOVA and Dunnet's multiple comparison test. Absolute p-values are indicated.



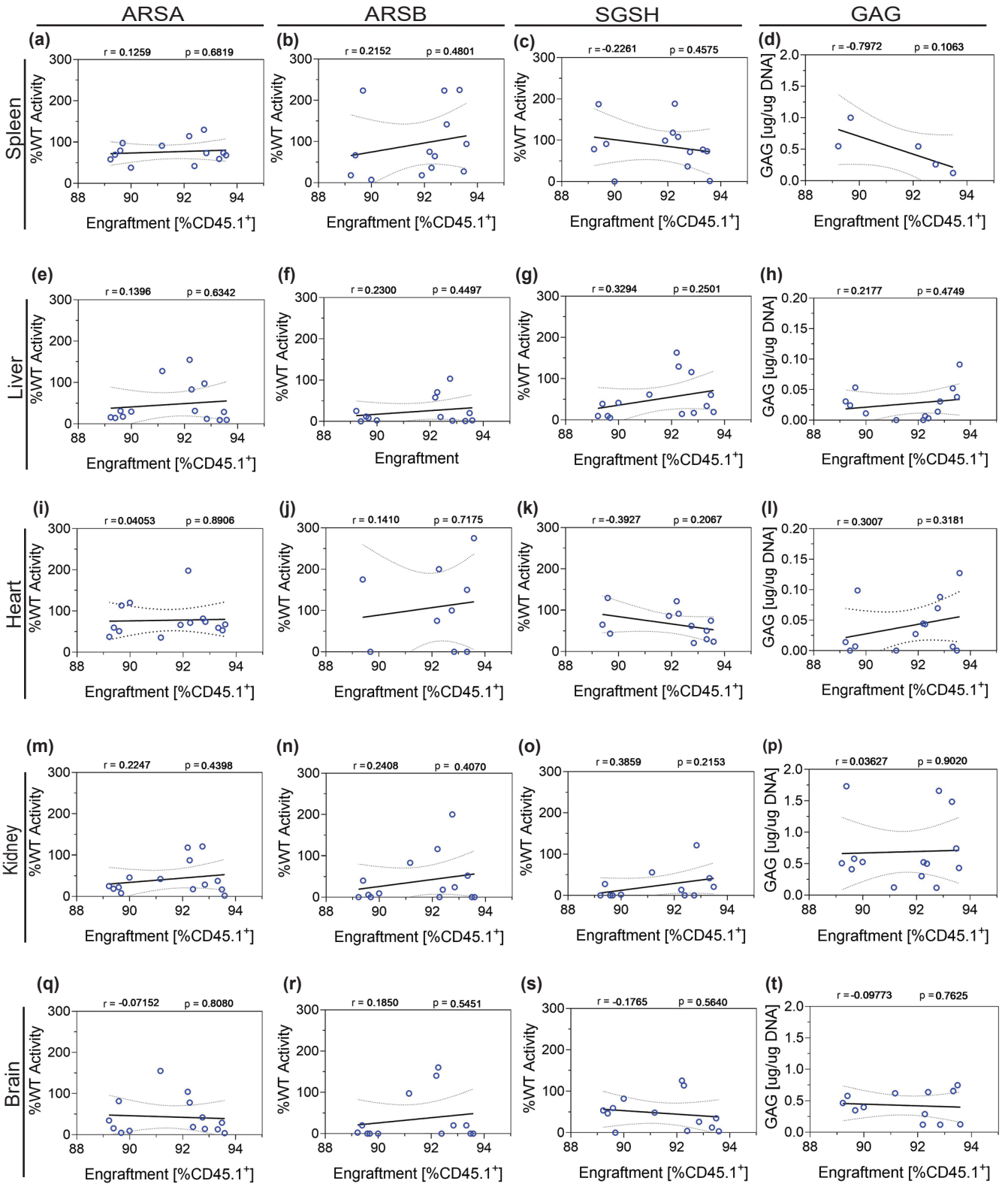
Supplementary Figure 3: Neurodegeneration analysis

NeuN⁺ immunohistochemistry on brain of Sumf1$^{+/+}$, and Sumf1$^{153/S153P}$, without bone marrow (BM) transplant or receiving either Sumf1$^{+/+}$ BM or Sumf1$^{S153/S153P}$ BM. Representative images of **a** hippocampus, **b** motor cortex, **c** visual cortex, **d** cerebellum. Representation of %Stained Area of NeuN⁺ in **e** Hippocampus (CA1), **f** Motor Cortex, **g** Visual Cortex, and **h** Cerebellum shown as mean ± SEM. Images from hippocampus and cortex at magnification X20, scale bar 50 µm. Scale bar for cerebellum: X40, 25 µm. Multiple comparaisons using Brown-Forsythe and Welch ANOVA tests. Absolute p-values are indicated.



Supplementary Figure 4: Irradiation preconditioning affected Rods response

Vision performance was assessed by ERG at 6 months post-BMT transplant on all experimental groups. **a** A-waves, and **b** B-waves amplitude response from rod cells is represented as the mean ± SEM (N=8-11), for each flash stimulous intensity. Sumf1$^{(+/+)}$ no-BMT was compared to Sumf1$^{(S153P)}$ + BMT-Sumf1$^{(+/+)}$,* p<0.05, ** p<0.01, **** p<0.0001; Sumf1$^{(S153P)}$ + BMT-Sumf1$^{(S153P)}$, ## p<0.01, ### p<0.001, #### p<0.0001; Sumf1$^{(+/+)}$ + BM$^{(+/+)}$, $$$$ p<0.0001; Sumf1$^{(S153P)}$ no-BMT, & p<0.05, && p<0.01; by 2-way ANOVA and Sidak multiple comparison test.



Supplemental Figure 5: Correlation Sulfatase activity, and GAG content vs Engraftment frequency
The frequency of donor derived CD45.1⁺ cells in peripheral blood leukocytes, is graphed vs the sulfatase activity for ARSA, ARSB, SGSH, and total GAG. Sulfatase activity is represented as percentaje of WT controls. Total GAG tissue content is represented as ug normalized to gDNA content. **a-d** Spleen, **e-h** Liver, **i-l** Heart, **m-p** Kidney, **q-t** Brain. For each pair comparison, the Pearson correlation coeficient (r) and the p-value (p) is reported. Each graph include a linear regresion model.