Supplementary Figures

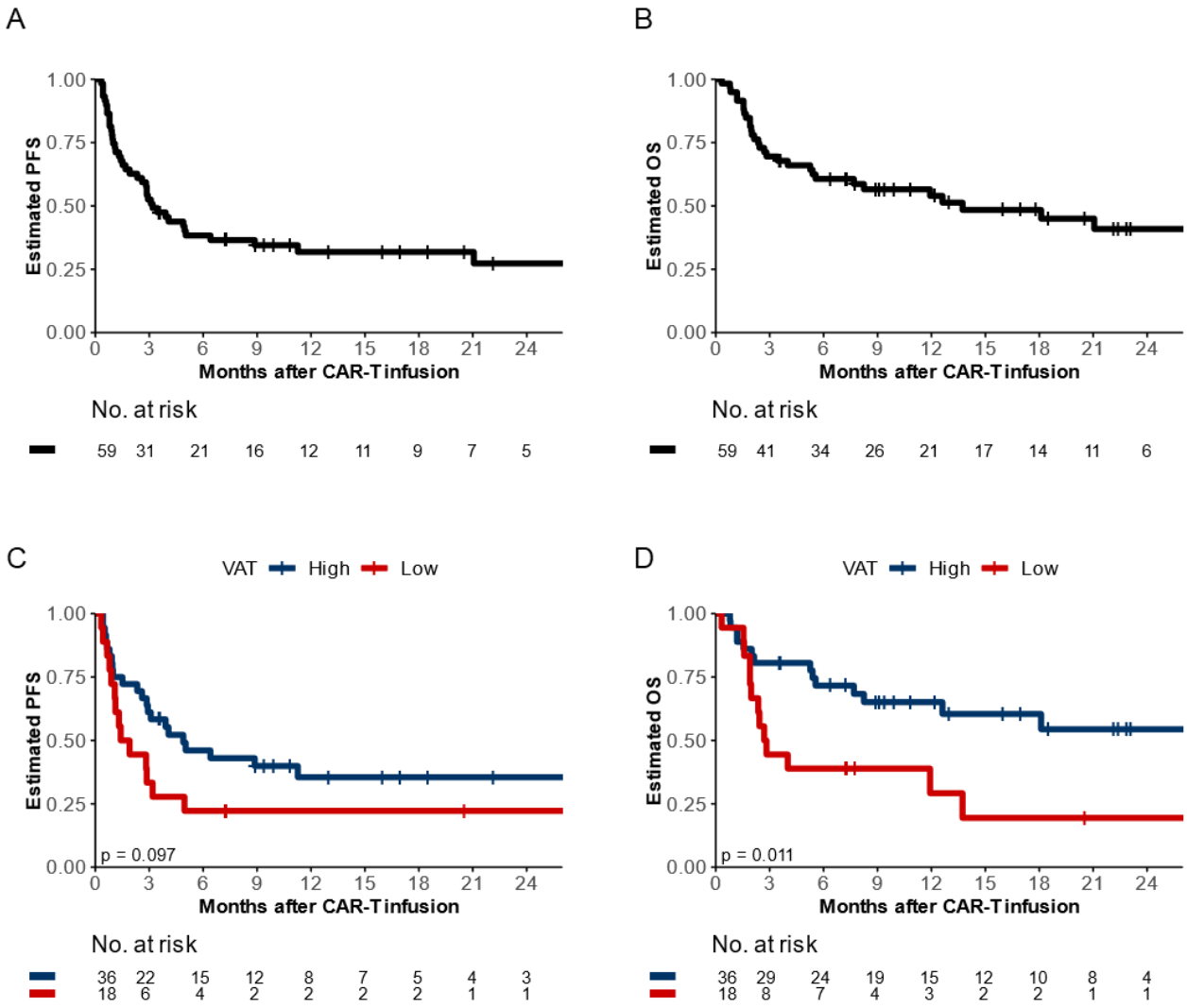

Figure S1. Survival outcomes of the discovery cohort stratified by visceral adipose tissue (VAT).
Kaplan–Meier curves for progression-free survival (PFS, panels A and C) and overall survival (OS, panels B and D) for the entire cohort (A/B) and stratified by visceral adipose tissue (C/D) based on previously published cutoffs. Statistical differences were assessed using the log-rank test.

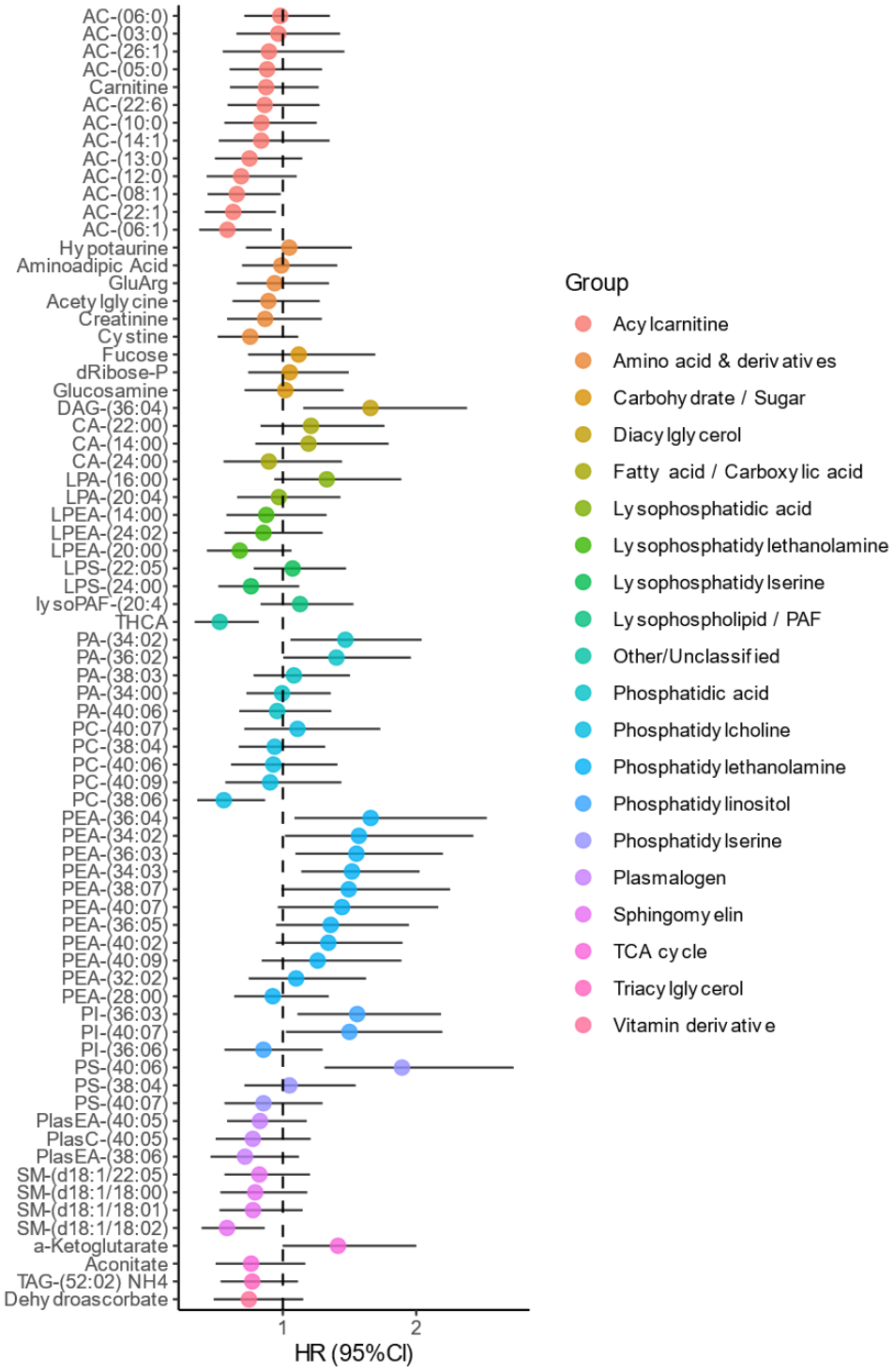

Figure S2. Serum metabolites associated with progression-free survival at baseline (Day 0).

Forest plot showing hazard ratios (HRs) and 95% confidence intervals (95% CIs) for serum metabolites identified through the feature selection process as associated with PFS. Metabolites are color-coded by biochemical class.

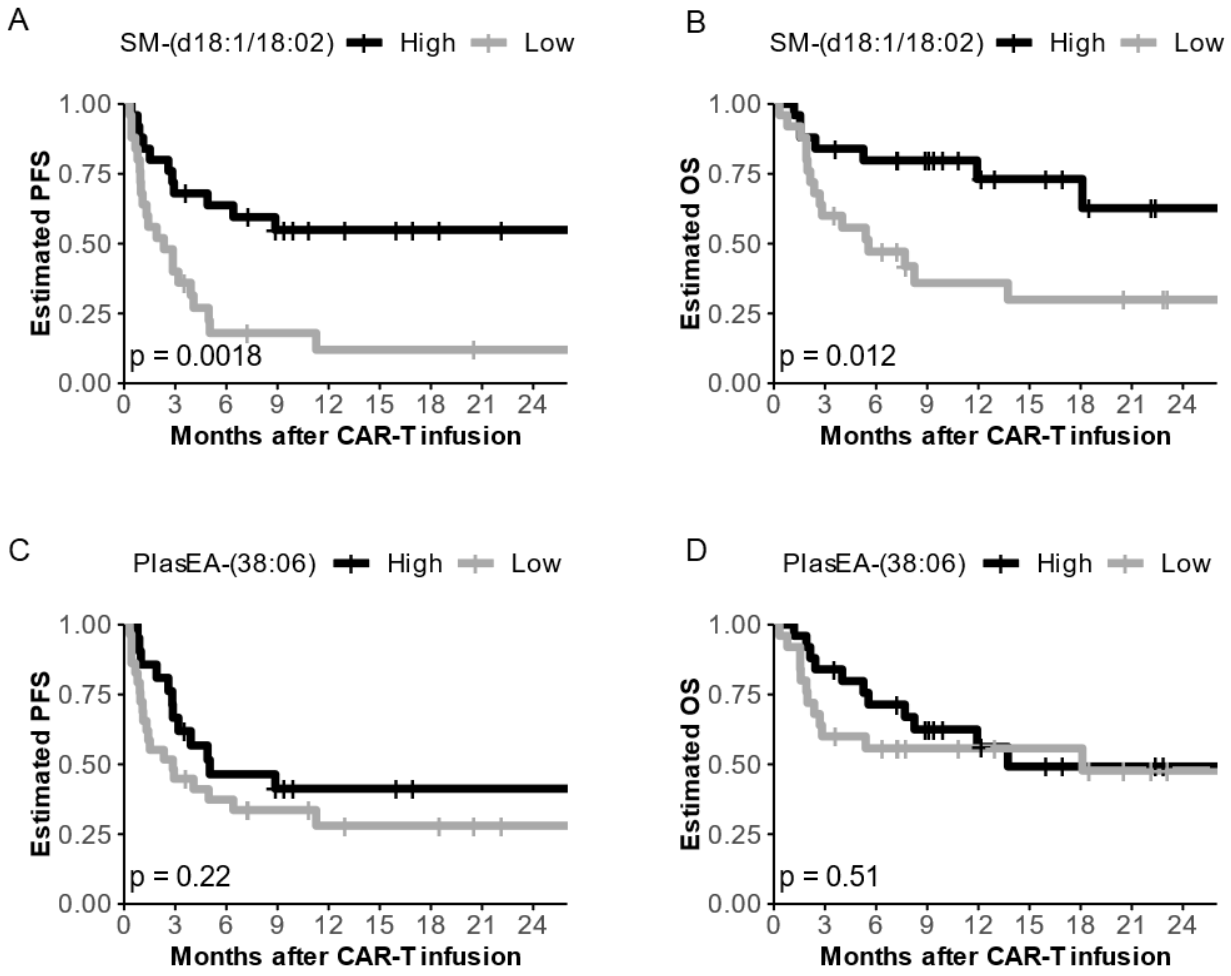

Figure S3. Association of sphingomyelins and plasmalogens with survival after CAR-T cell therapy.

Kaplan–Meier curves for PFS (panels A and C) and OS (panels B and D) were stratified by median serum levels of representative metabolites: SM (d18:1/18:02) was used as a marker for sphingomyelins and PlasEA (38:06) for plasmalogens. Statistical significance was evaluated using the log-rank test.

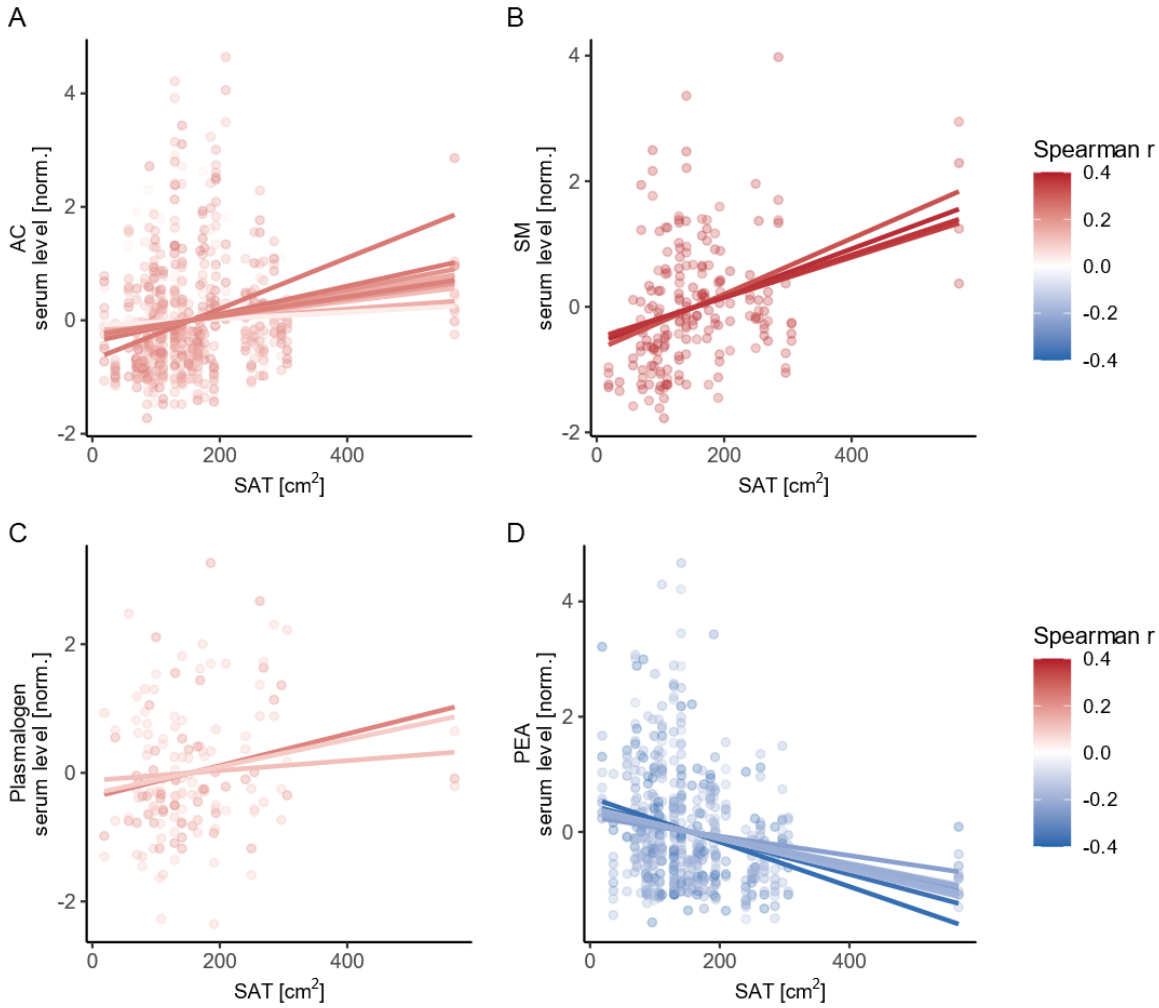

Figure S4. Correlation between identified serum lipids and subcutaneous adipose tissue. Scatter plots with linear regression overlays show Spearman correlation coefficients between normalized serum lipid levels and subcutaneous adipose tissue (SAT) measured at baseline (Day 0), grouped by lipid class. The color gradient represents the strength and direction of the correlation.

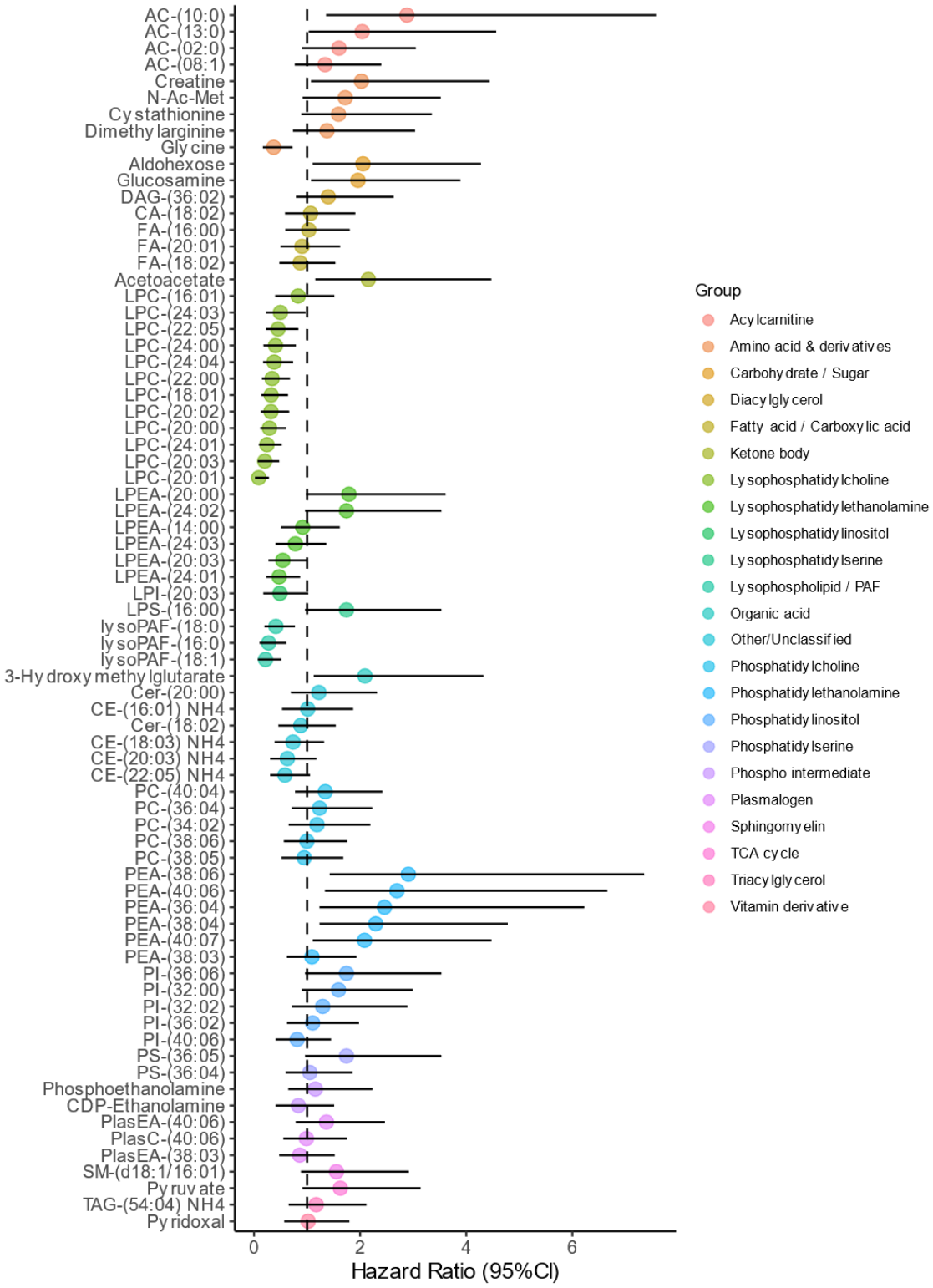

Figure S5. Association between serum metabolites at Day 3–5 and CRS severity.
Forest plot showing odds ratios (ORs) and 95% confidence intervals (95% CIs) for serum metabolites identified by feature selection as associated with grade ≥2 cytokine release syndrome (CRS) at Day 3–5 post-CAR-T cell infusion. Metabolites are color-coded by biochemical group.

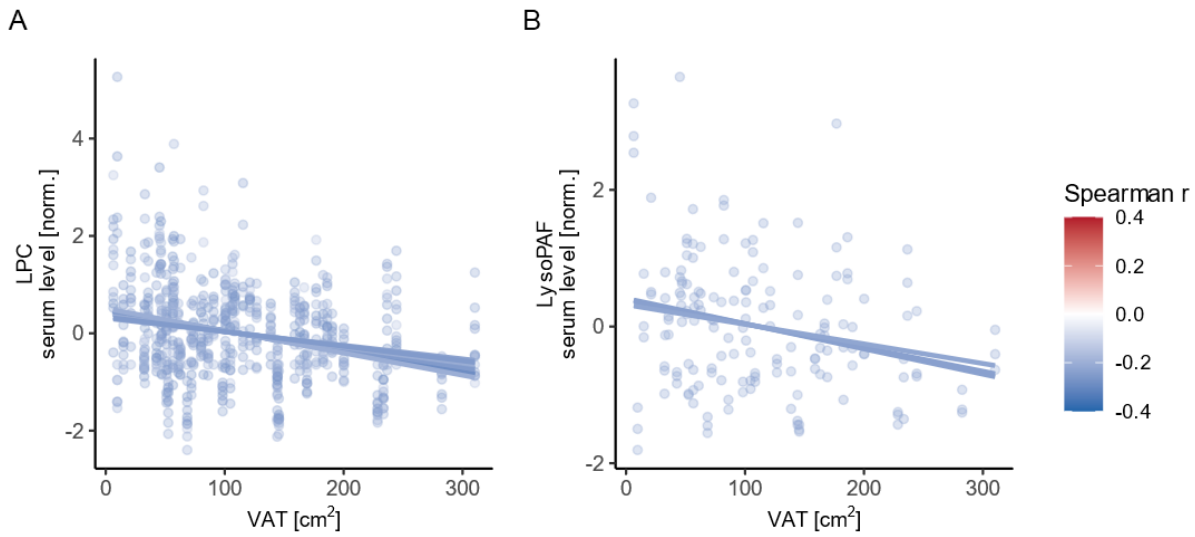

Figure S6. Negative correlations of lysophosphatidylcholines and lyso PAFs with visceral adipose tissue.

Scatter plots with linear regression overlays depicting Spearman correlations between normalized serum levels of (A) lysophosphatidylcholines and (B) lyso platelet-activating factors (lyso PAFs) and VAT at Day 3–5 post-infusion. Color gradient reflects correlation coefficients by lipid group.

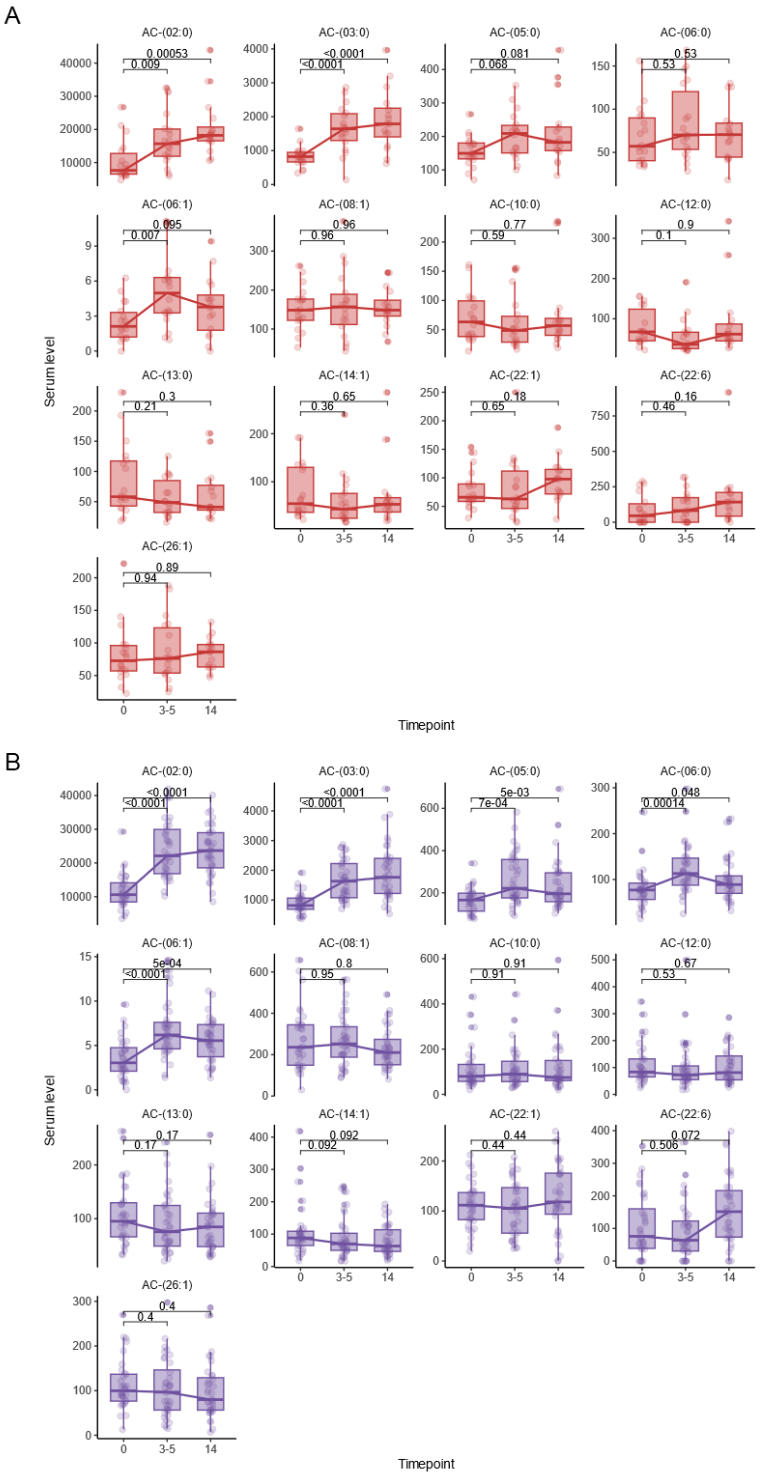

Figure S7. Temporal dynamics of serum acylcarnitines stratified by VAT.
Boxplots illustrating serum acylcarnitine (AC) levels at baseline (Day 0), early (Day 3–5), and intermediate (Day 14) time points after CAR-T therapy, stratified by low (A) vs high (B) visceral adipose tissue (VAT). Points represent individual measurements; boxes indicate median and 95%

confidence interval. Lines connect median values across time. Statistical comparisons were performed using the Wilcoxon signed-rank test, with Day 0 as the reference.

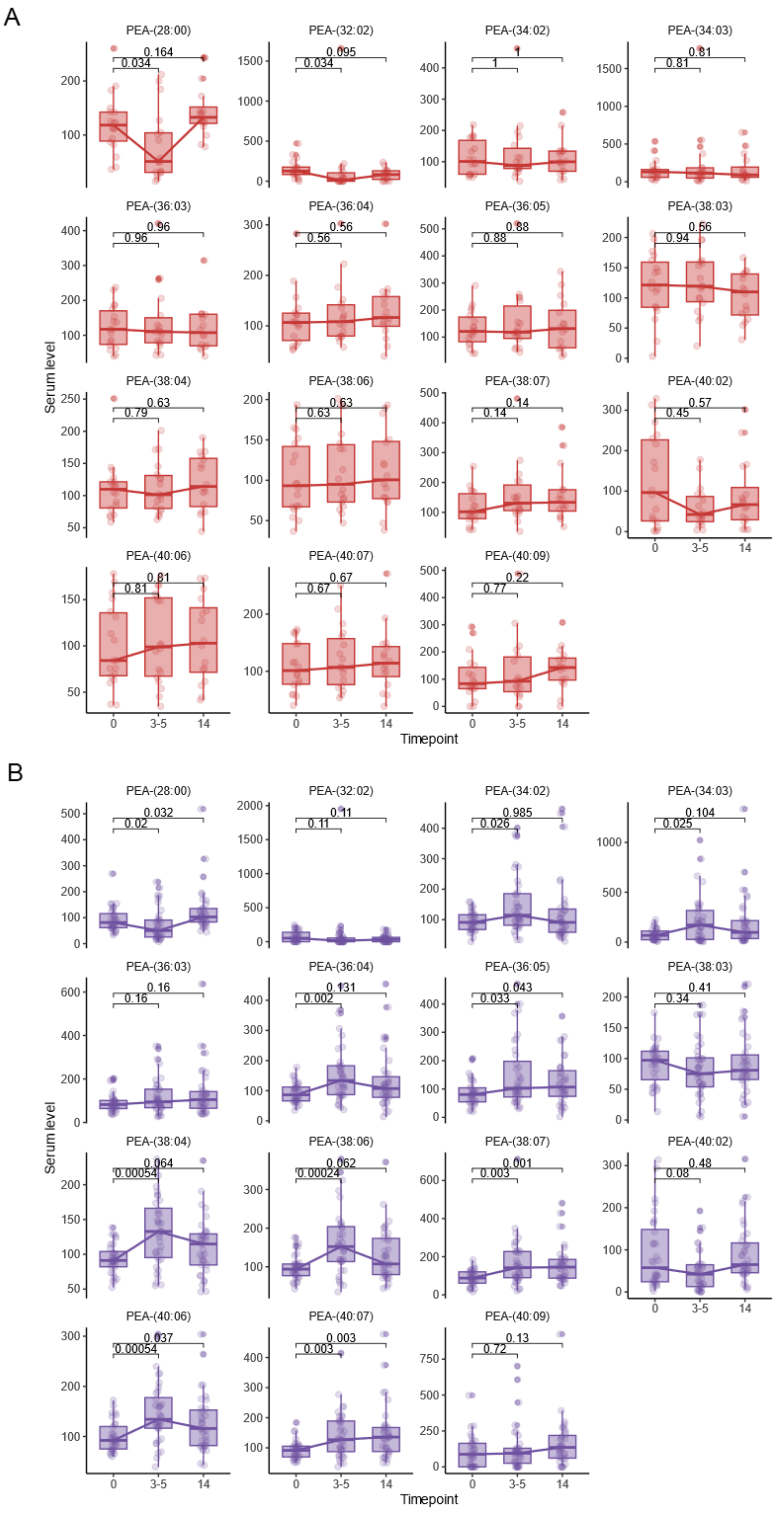

Figure S8. Temporal dynamics of serum phosphatidylethanolamines stratified by VAT. Boxplots showing serum phosphatidylethanolamine (PEA) levels at baseline, early (Day 3–5), and intermediate (Day 14) time points after CAR-T therapy, stratified by low (A) and high (B) VAT. Individual measurements are shown as points. Median and 95% CI are indicated; medians are connected by lines. Statistical comparisons were performed using the Wilcoxon signed-rank test, with Day 0 as the reference.

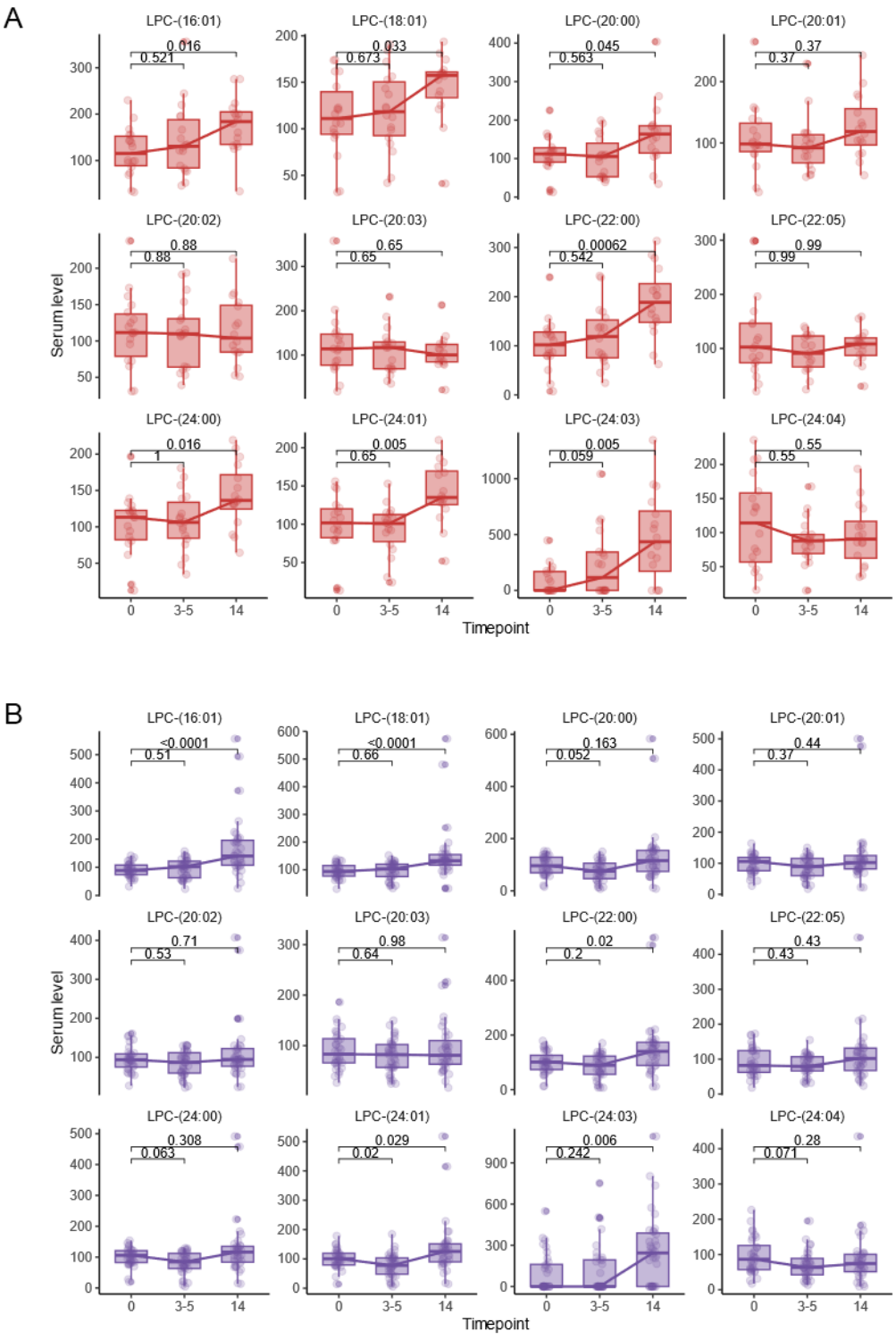

Figure S9. Temporal dynamics of serum lysophosphatidylcholines stratified by VAT. Boxplots depicting serum lysophosphatidylcholine (LPC) levels at baseline, early (Day 3–5), and intermediate (Day 14) post-infusion in patients with low (A) or high (B) VAT. Points indicate individual values; boxplots show median and 95% CI. Lines connect median values across time points. Statistical comparisons were performed using the Wilcoxon signed-rank test, with Day 0 as the reference.

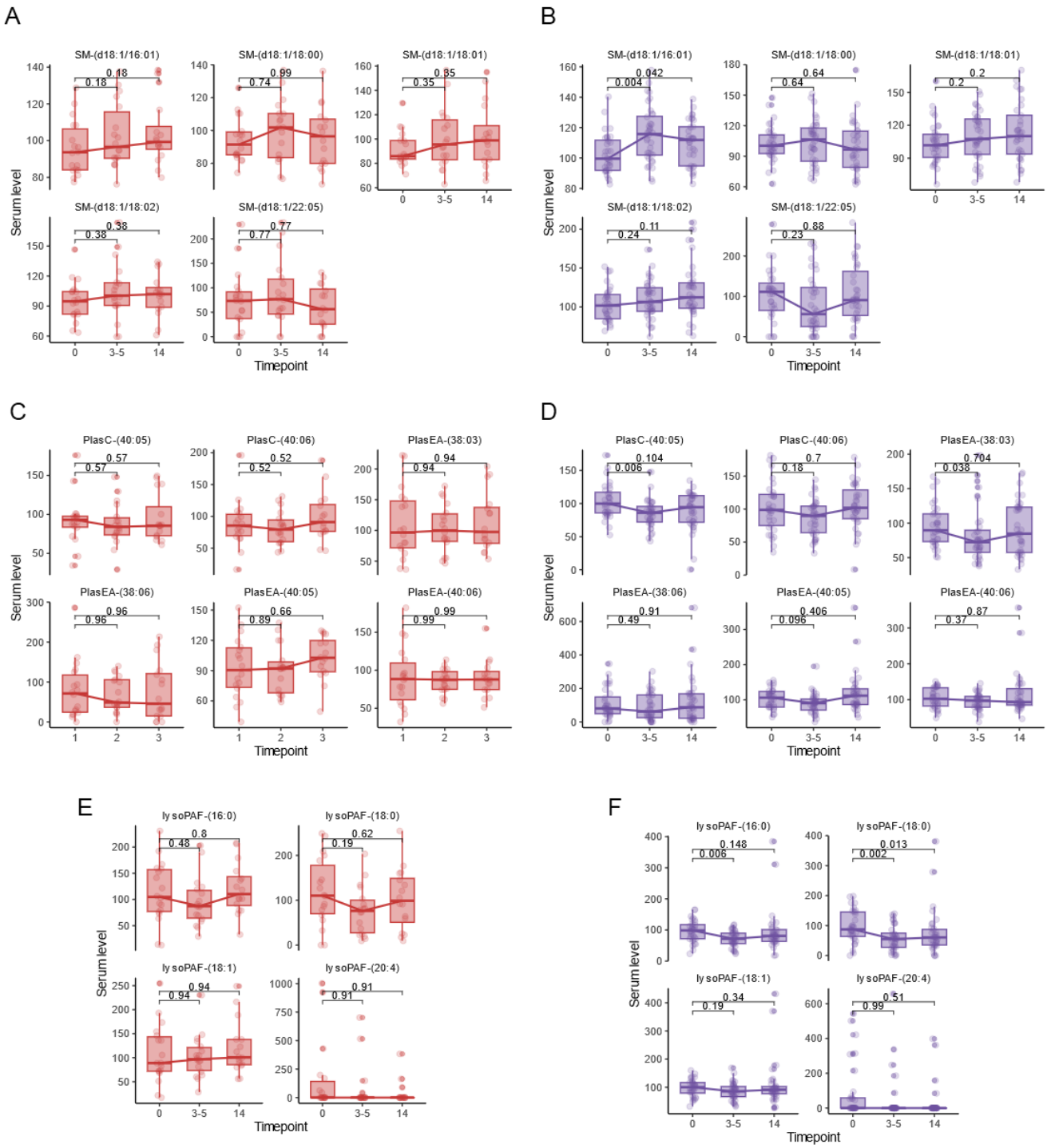

Figure S10. Longitudinal serum dynamics of SMs, plasmalogens, and lysoPAFs by VAT. Boxplots showing temporal changes in serum sphingomyelins (SMs, panels A/B), plasmalogens (Plas, panels C/D), and lysophosphatidylacetyltransferases (lysoPAFs, panels E/F) at baseline, Day 3–5, and Day 14 post-CAR-T therapy in patients with low (A/C/E) or high (B/D/F) VAT. Points represent individual values; boxes show median and 95% CI; lines connect medians. Statistical comparisons were performed using the Wilcoxon signed-rank test, with Day 0 as the reference.

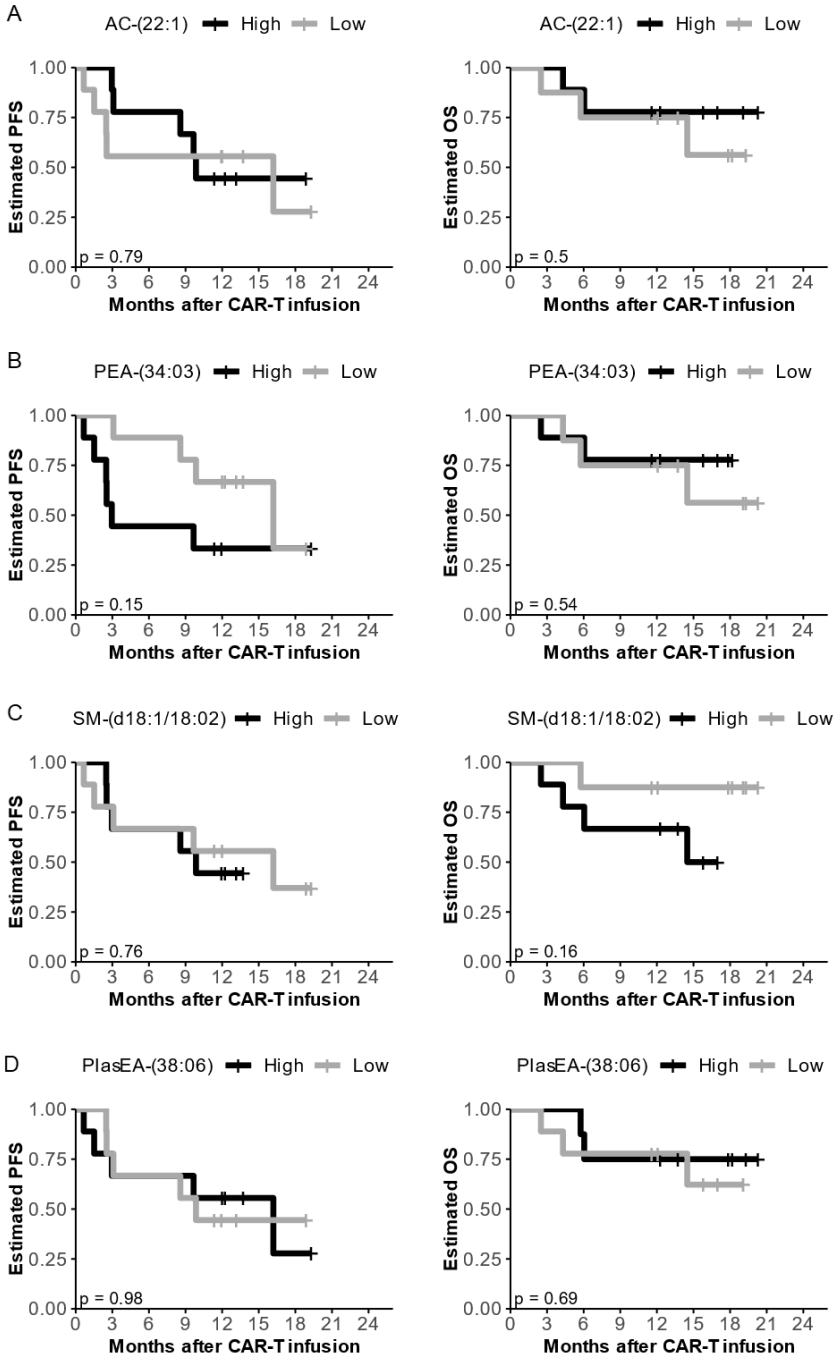

Figure S11. Serum lipid levels at lymphodepletion do not predict survival in the validation cohort.

Kaplan–Meier plots for PFS (left) and OS (right) in the validation cohort, stratified by median serum levels of metabolites previously associated with survival in the discovery cohort. Representative lipids include: (A) AC-(22:2) for acylcarnitines, (B) PEA-(34:03) for phosphatidylethanolamines, (C) SM-(d18:1/18:02) for sphingomyelins, and (D) PlasEA-(38:06) for plasmalogens. Lipids were measured at the time of lymphodepletion (Day -6). High vs. low groups were defined by the cohort-specific medians. Log-rank test was used to assess survival differences.

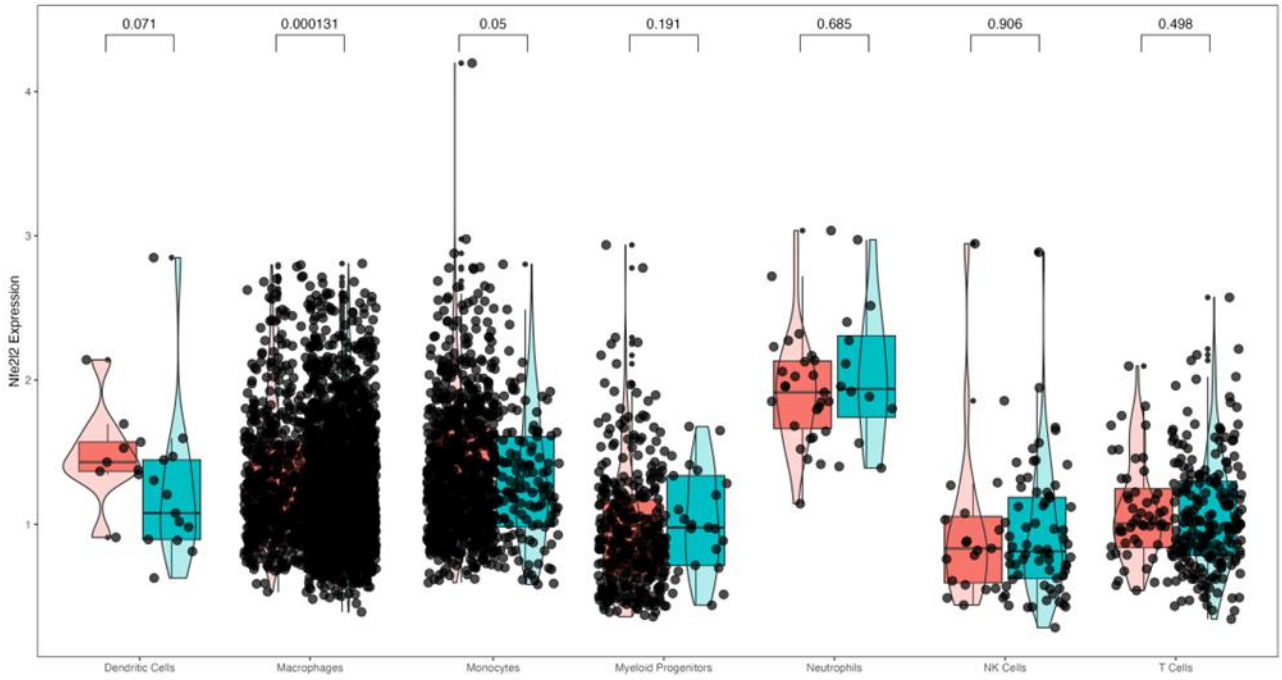

Figure S12. Expression of *Nfe2l2* in bone marrow cell subsets.
Boxplots depict *Nfe2l2* expression in single-cell RNA-seq data comparing adipocyte-cocultured versus control bone marrow cells. A trend toward higher expression in adipocyte-cocultured (orange) versus fibroblast-cocultured (turquoise) cells was observed (macrophages, monocytes, dendritic cells). Boxes indicate the interquartile range (IQR), whiskers the 1.5×IQR, and horizontal lines the median. Statistical testing was performed using Student's t-test with correction for multiple testing using FDR.

Supplementary Tables

Table S1 Baseline characteristics of the discovery cohort.

	Discovery cohort (n=54)
Basic Characteristics	
Sex, female – n (%)	20 (37.0)
Age – median (range)	61 (19-82)
Entity – n (%)	
- DLBCL	50 (58.8)
- MCL	4 (17.6)
Costimulatory domain – n (%)	
- 41BB	28 (51.9)
- CD28z	26 (48.1)
Body composition – median (IQR)	
BMI [kg/m^2]	23.4 (21.8-26.7)
Waist [cm]	99.2 (89.3-129.1)
SAT [cm^2]	140 (98.9-192.2)
VAT [cm^2]	99.4 (53.4-162.1)
STLV [mL]	87.8 (13.8-365.4)
Lab values at LD – median (IQR)	
Leukocytes [G/L]	3.8(2.2-5.2)
Ferritin [ng/mL]	694 (238-1427)
LDH [U/L]	273 (195-451)
CRP [mg/L]	1 (0.2-3.0)

Abbreviations: 41BB, CD137 costimulatory domain; BMI, body mass index; CD28z, CD28 costimulatory domain with ζ signaling; CRP, C-reactive protein; DLBCL, diffuse large B-cell lymphoma; LD, lymphodepletion; LDH, lactate dehydrogenase; MCL, mantle cell lymphoma; SAT, subcutaneous adipose tissue; STLV, skeletal muscle tissue volume; VAT, visceral adipose tissue.

Table S2 Baseline characteristics of the validation cohort.

	Validation cohort (n=17)
Basic Characteristics	
Sex, female – n (%)	5 (29.4)
Age – median (range)	65 (38-85)
Entity – n (%)	
- DLBCL	10 (58.8)
- MCL	3 (17.6)
- MM	4 (23.5)
Costimulatory domain – n (%)	
- 41BB	6 (35.3)
- CD28z	11 (64.7)
Body composition – median (IQR)	
BMI [kg/m^2]	27 (23.3-30.4)
Waist [cm]	93.8 (90.4-108)
SAT [cm^2]	185 (138-254)
VAT [cm^2]	160 (105-245)
STLV [mL]	32.8 (13.4-60.6)
Lab values at LD – median (IQR)	
Leukocytes [G/L]	3.54 (2.67-5.98)
Ferritin [ng/mL]	204 (139-246)
LDH [U/L]	115 (52.5-469)
CRP [mg/L]	0.3 (0.3-2.8)

Abbreviations: 41BB, CD137 costimulatory domain; BMI, body mass index; CD28z, CD28 costimulatory domain with ζ signaling; CRP, C-reactive protein; DLBCL, diffuse large B-cell lymphoma; LD, lymphodepletion; LDH, lactate dehydrogenase; MCL, mantle cell lymphoma; SAT, subcutaneous adipose tissue; STLV, skeletal muscle tissue volume; VAT, visceral adipose tissue.