A

rank = 2   rank = 3   rank = 4

rank = 5   rank = 6   rank = 7

B

x^2Pearson(1) = 11.11 , p = 8.58e-04

icu
yes
no

cluster1 (n = 64)   cluster2 (n = 36)
PYRcluster

62% 38%   28% 72%

C

x^2Pearson(1) = 0.10 , p = 0.75

diabetes mellitus
yes
no

cluster1 (n = 63)   cluster2 (n = 36)
PYRcluster

37% 63%   33% 67%

D

x^2Pearson(1) = 0.32 , p = 0.57

Sex
male
female

cluster1 (n = 64)   cluster2 (n = 36)
PYRcluster

64% 36%   58% 42%

E

Wilcoxon, p=0.68

age(year)

cluster1   cluster2
PYRcluster

Figure 1: (A) Consensus clustering matrix for k = 2-7 revealed that clustering performance was optimized when k=2 (B, C, D, E), with no significant differences in the proportion of ICU, diabetes mellitus, sex, and age between the two PYRclusters.
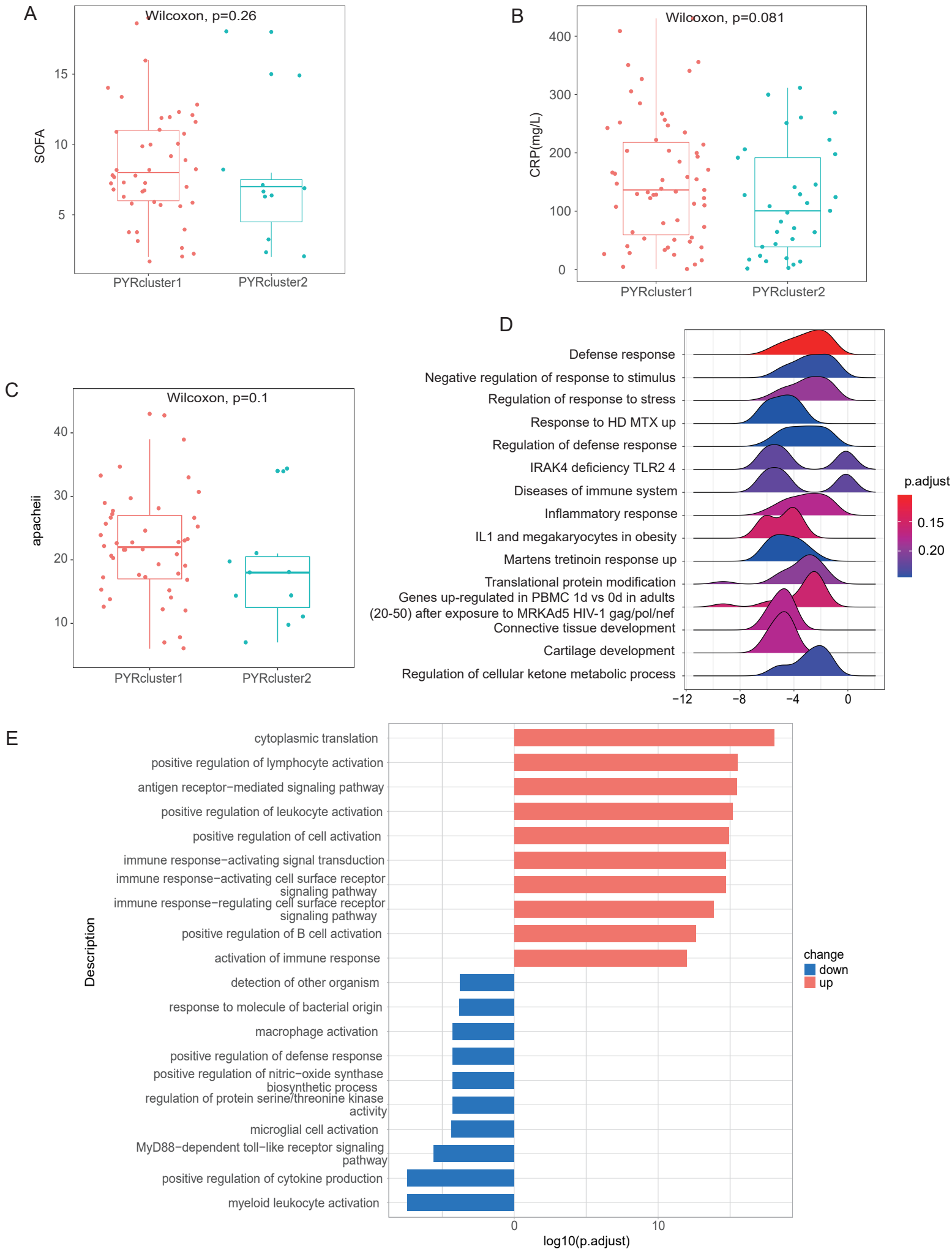
Supplementary figure 1

Figure 2: (A, B, C) SOFA, APACHE-II, and C-reaction protein (CRP) levels show no differences. (D) Ridgeline plot showing the expression distribution of GSEA results of 736 proteins. (E) Gene Ontology (GO) enrichment of 570 DEGs between the two PYRclusters; "up" means that these pathways of PYRcluster2 were upregulated when compared with PYRcluster1, and "down" means that these pathways were downregulated. ns, no significance.
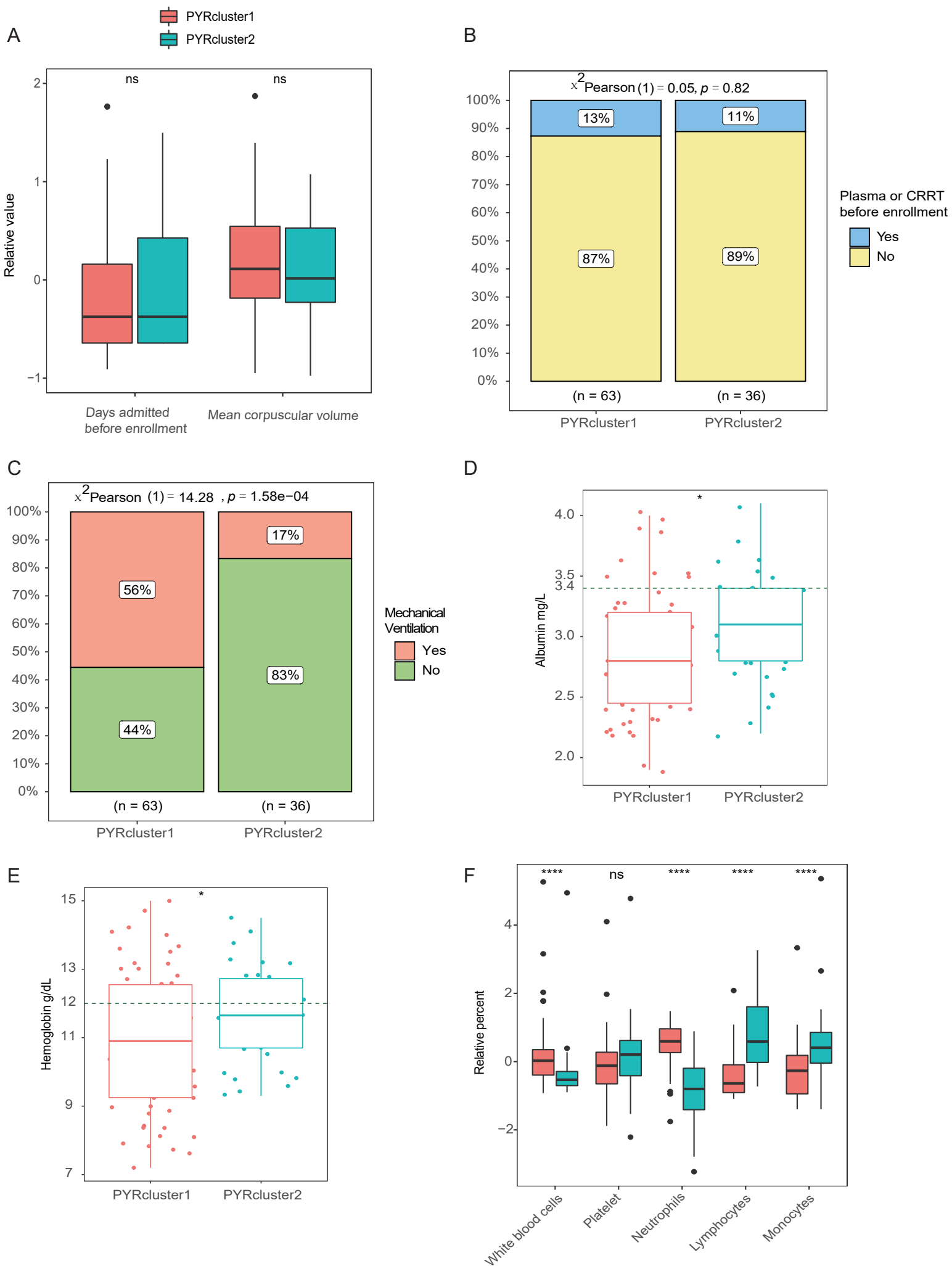
Supplementary figure 2

Figure 3: (A) Days admitted before enrollment and mean corpuscular volume of the 2 PYRclusters. (B, C) Percentage of replacement therapy (pre-enrollment) (B) or mechanical ventilation (C) patients in the 2 PYRclusters. (D, E) Blood levels of albumin (D) or hemoglobin in blood. (E) Relative percentage of different cells based on the hemogram results in the 2 PYRclusters. *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001, ns, no significance (Wilcoxon signed-rank test).
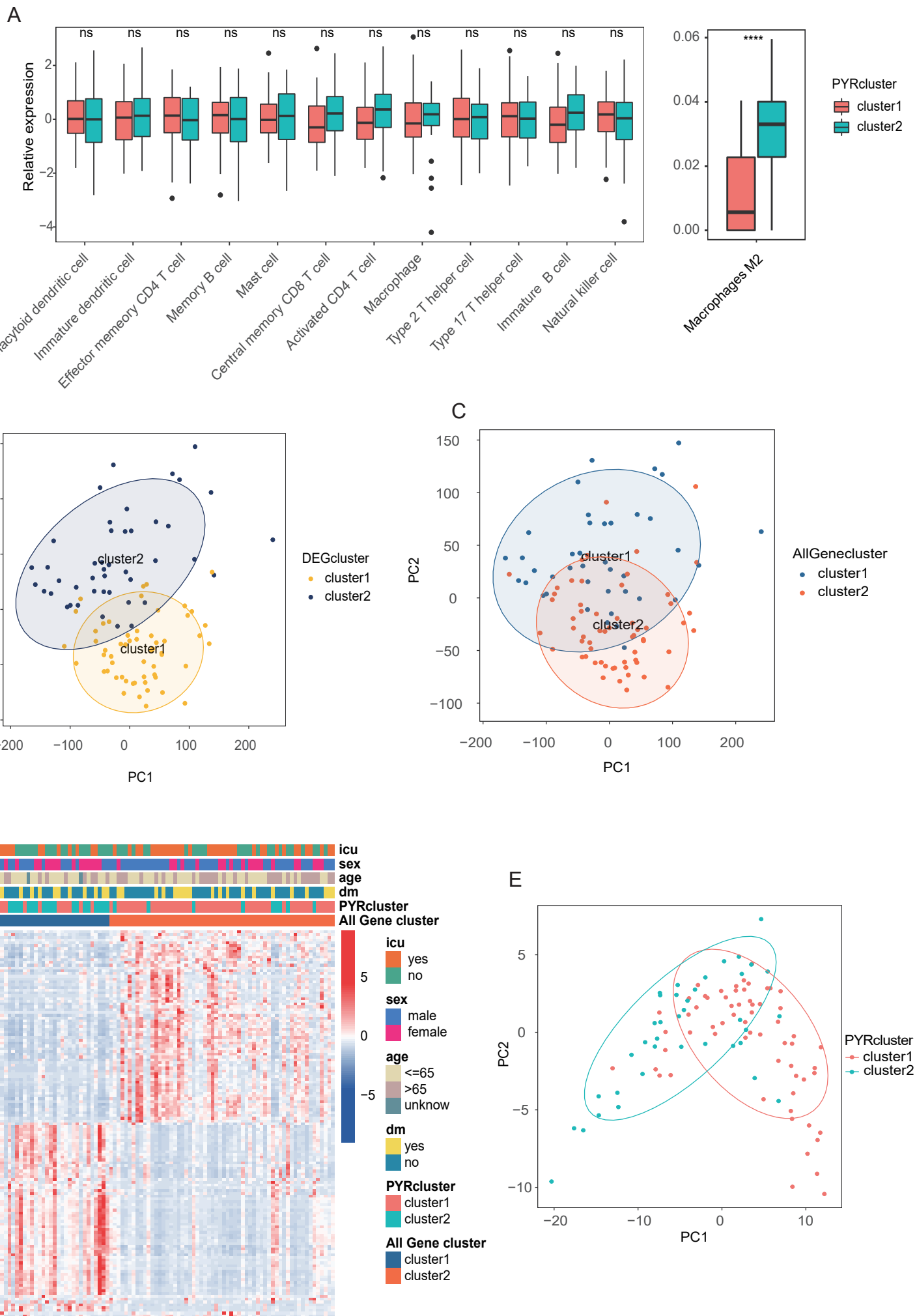
Figure 4: (A) Leukocyte counts, with no significant differences between PYRclusters. (B) PCA of DEGclusters. (C) PCA of All-Gene clusters. (D) DEGs between All-Gene clusters; once these new DEGs between different gene clusters were determined, their heatmap was plotted, showing varied clinical data in the annotation. (E) PCA used to construct the pyrscore.
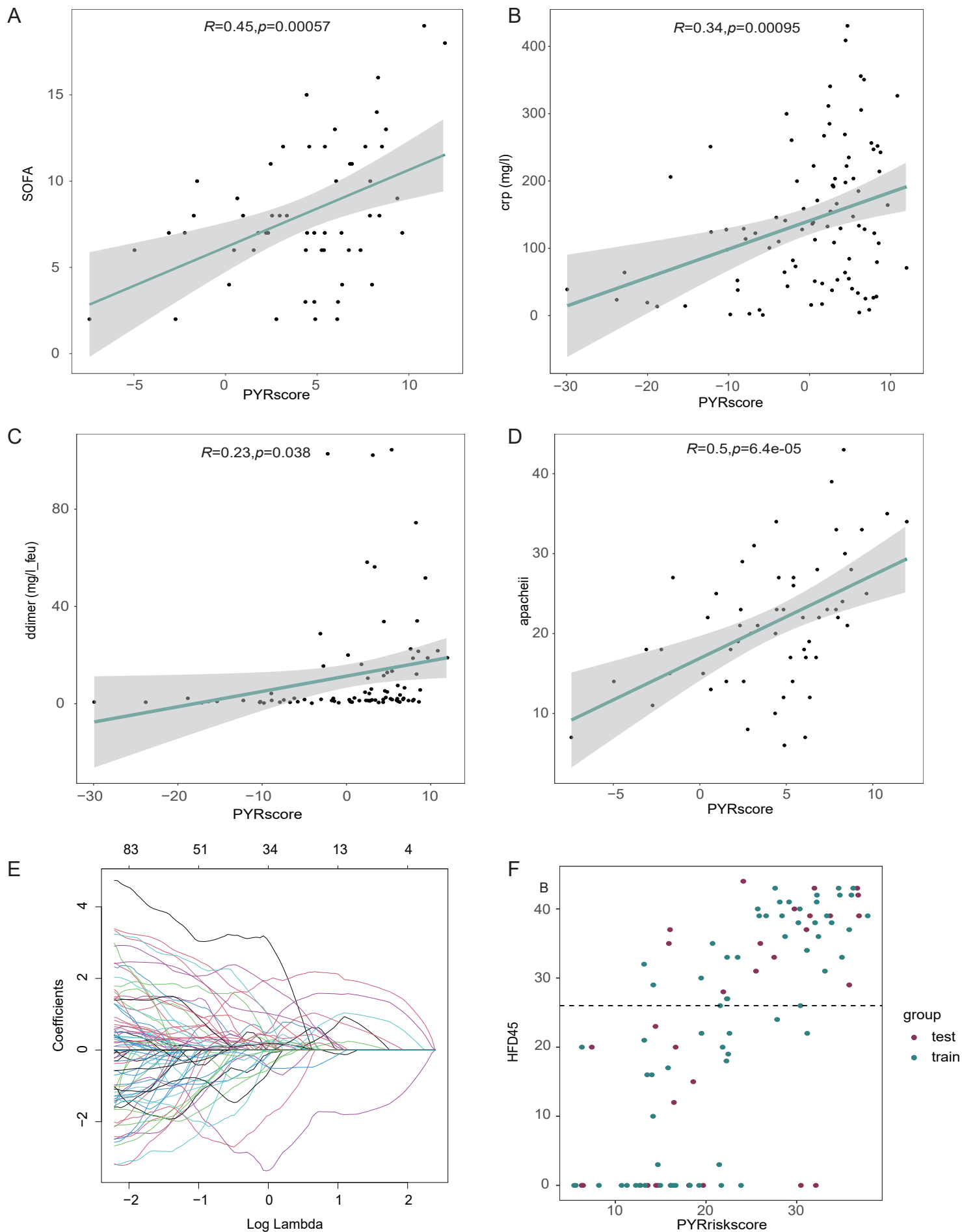
Supplementary figure 4

Figure 5: (A, B, C, D) Pearson product-moment correlations between pyrscore and sofa score (A), CRP levels (B), D-dimer levels (C), and APACHE-II (D), with the R value representing the Pearson product-moment correlation coefficient, and the grey area representing the 95% confidence interval for the linear fit. (E) LASSO coefficient profiles. (F) Correlations between PYRsafescore and HFD45 in different groups. The dotted line represents the median value of HFD45 (26).
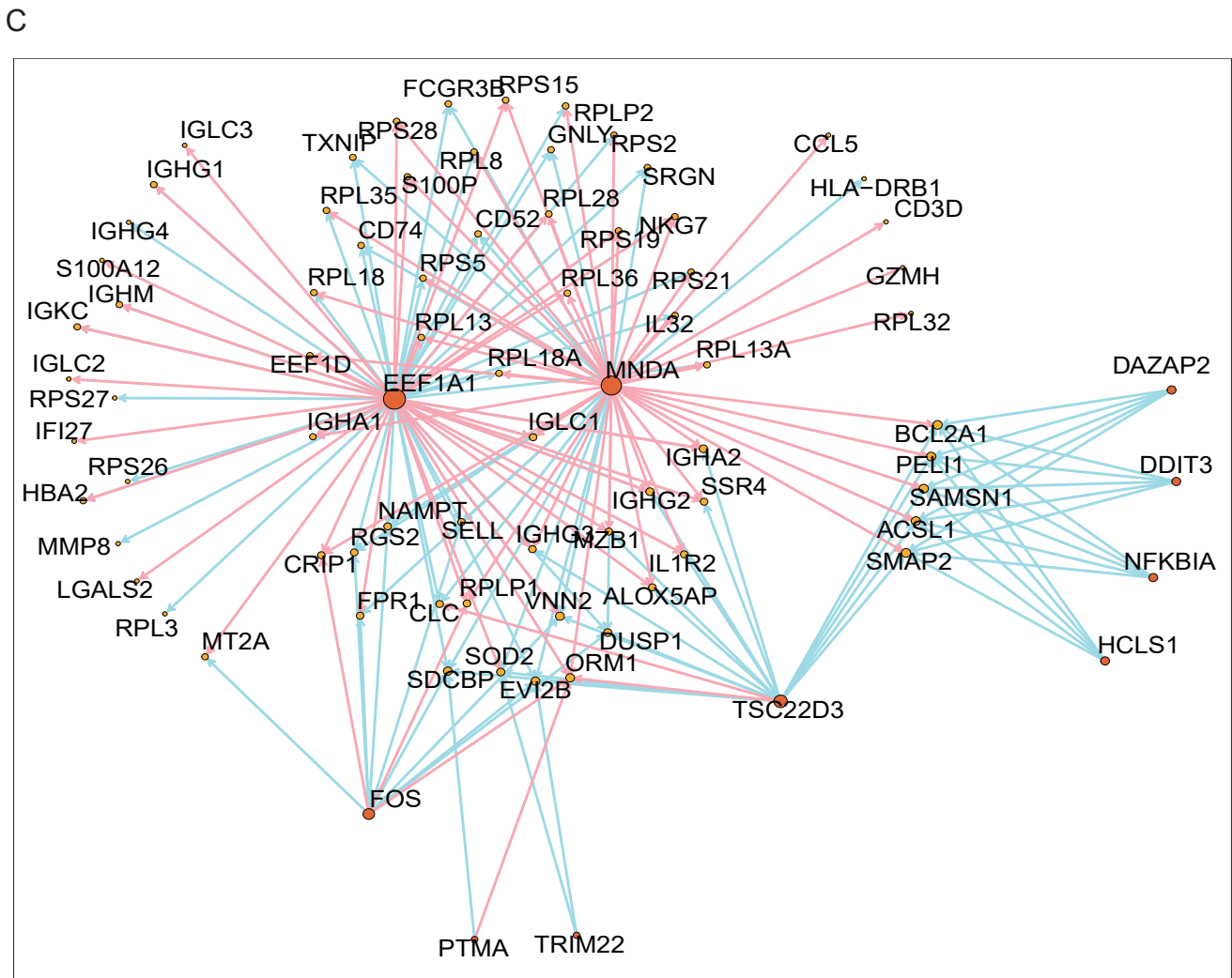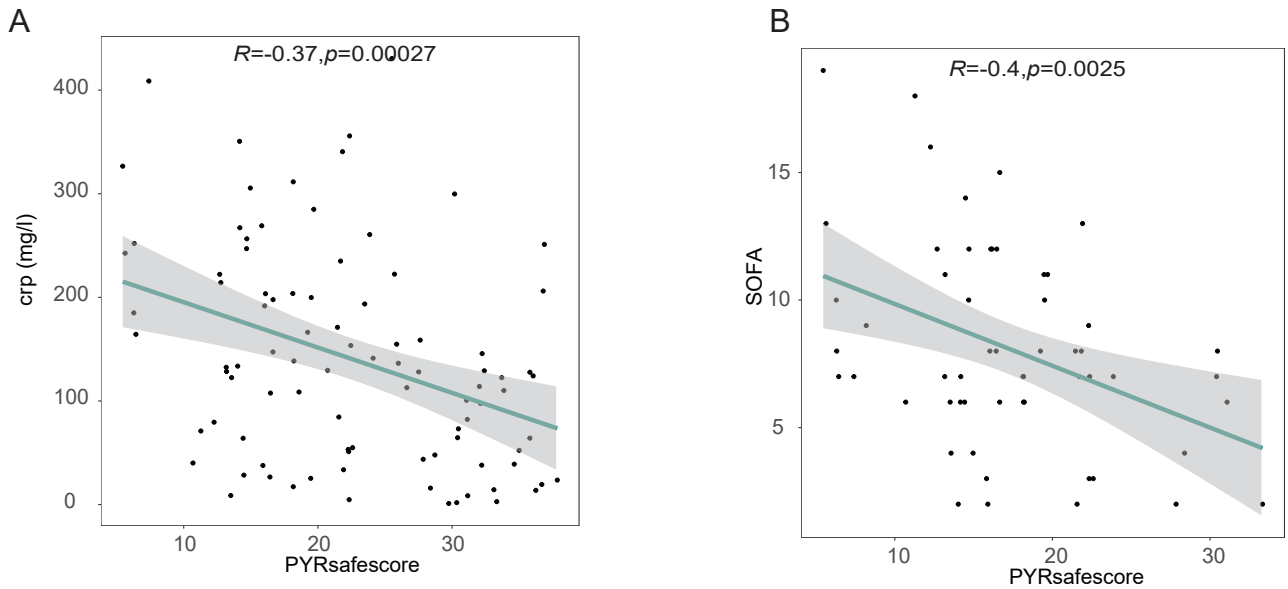
Supplementary figure 5

Figure 6: (A, B) Pearson product-moment correlations between PYRsafescore CRP levels (A) and SOFA (B), with the R value representing the Pearson product-moment correlation coefficient, and the grey area representing the 95% confidence interval for the linear fit. (C) Transcription factors regulatory network of PYRcluster2; "degree" means the number of edges connected to each node.