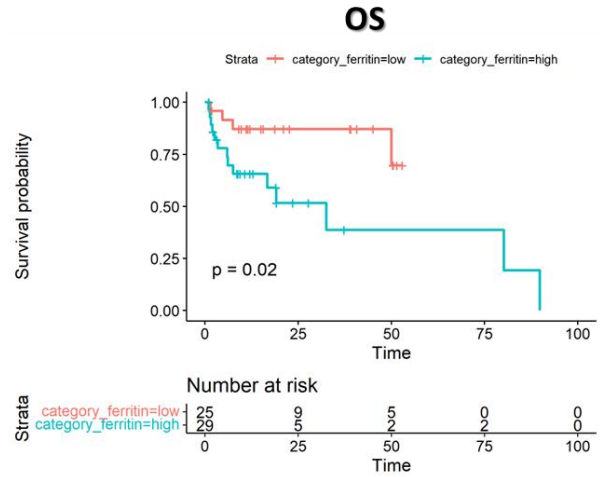
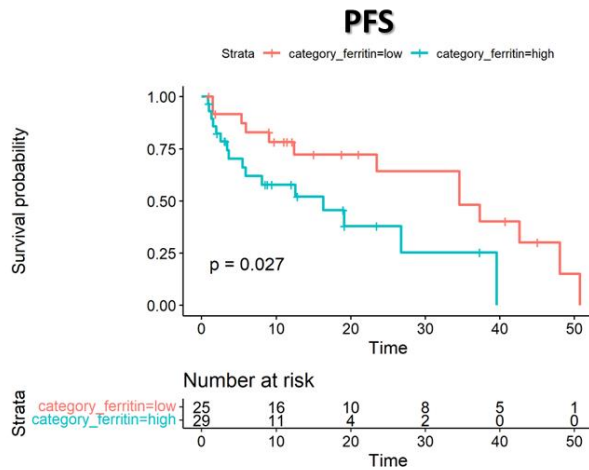
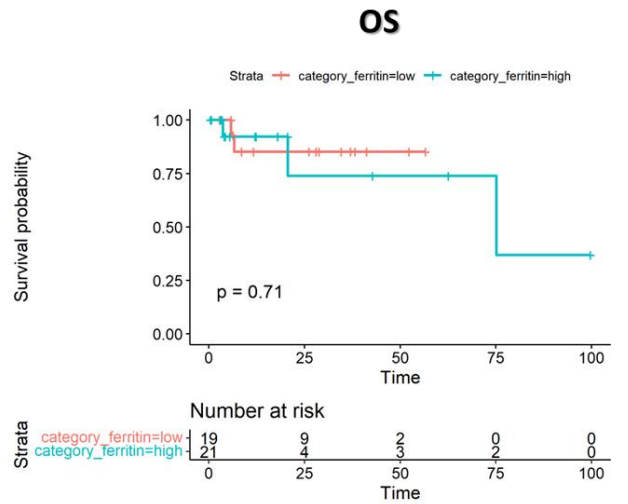
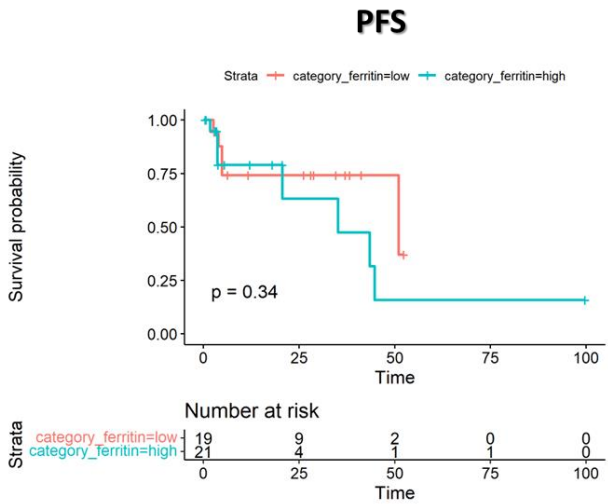


Supplementary Materials

ASCT-ineligible

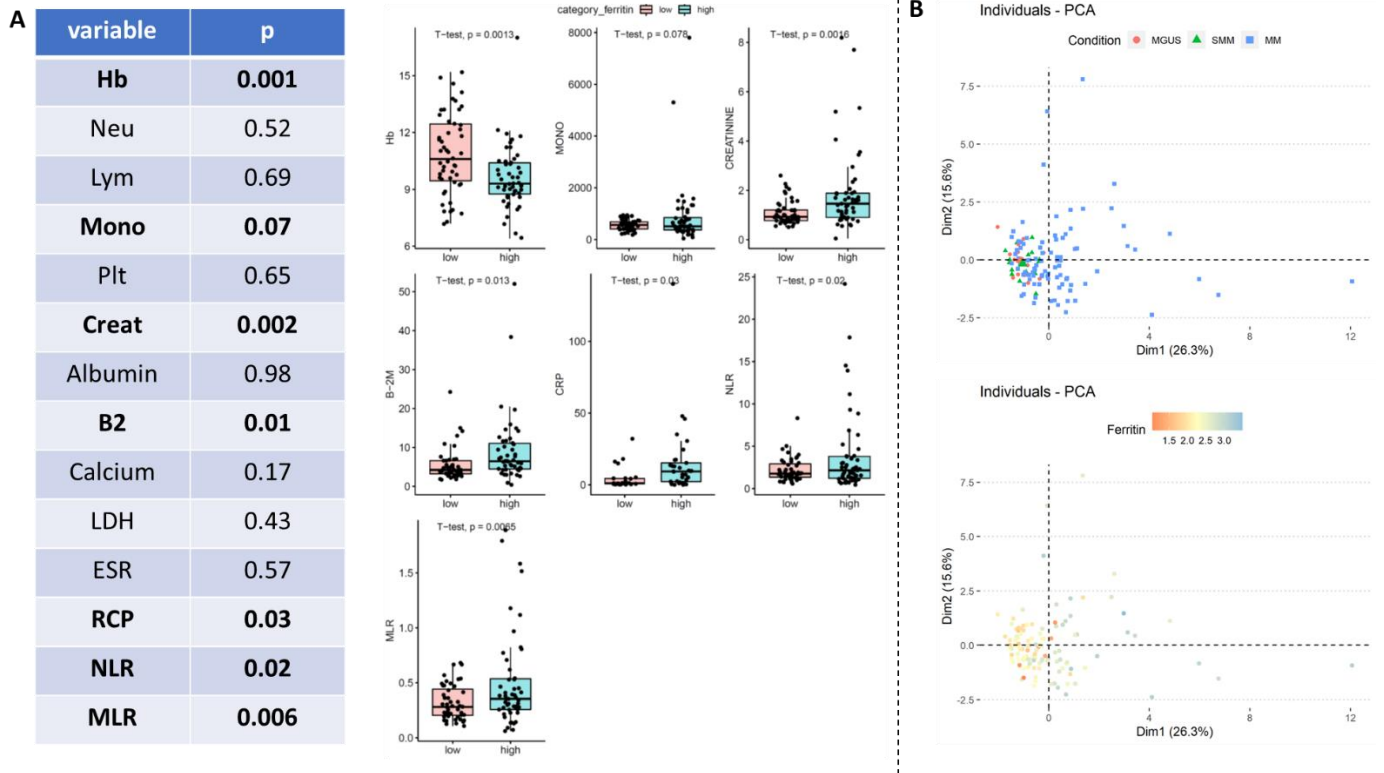


ASCT-eligible



Supplementary Figure S1: survival according to ASCT eligibility and ferritin values

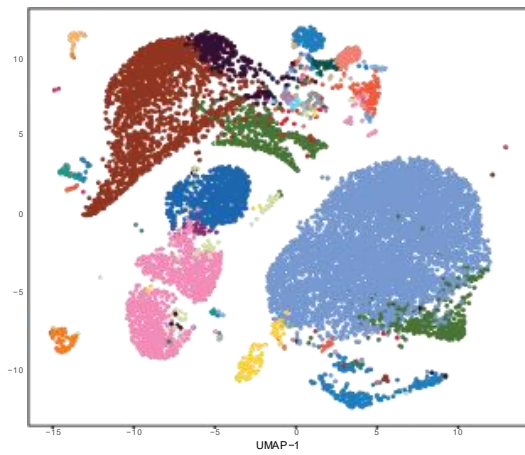
PFS and OS results for MM patients according to their transplant eligibility status. Please note that a significant value at the log-rank test was reached for ASCT-ineligible patients only.



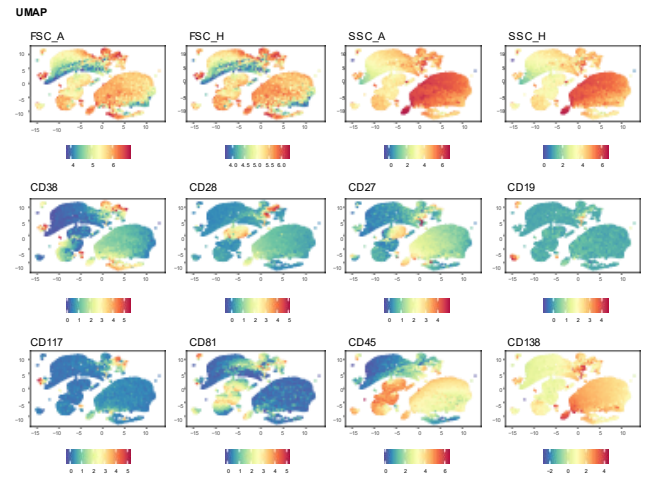
Supplementary Figure S2: correlation of laboratory variables with high/low levels of ferritin

A. Left: list of all variables tested for differences between high and low level ferritin groups and their p values according to t-Student test. On the right boxplots showing the results of the variable reaching a statistical significance. **B.** principal component analysis performed on significant values in MGUS, SMM and MM patients. Interestingly, all MGUS and SMM clusterize closer to the group of low ferritin MM patients.

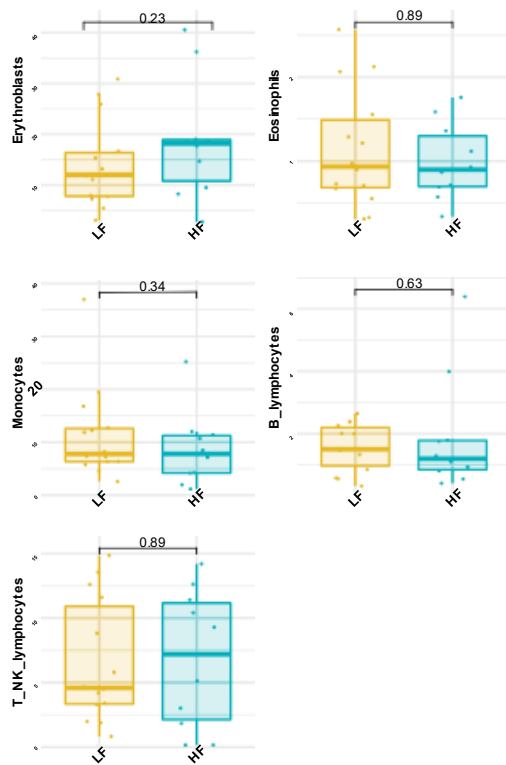
A



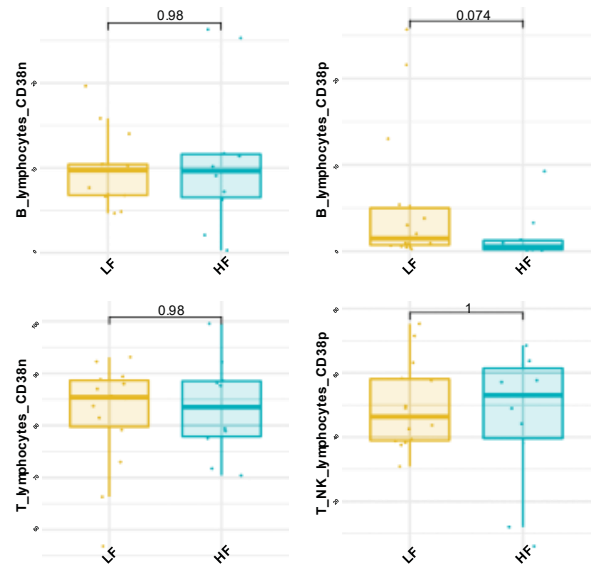
B



C

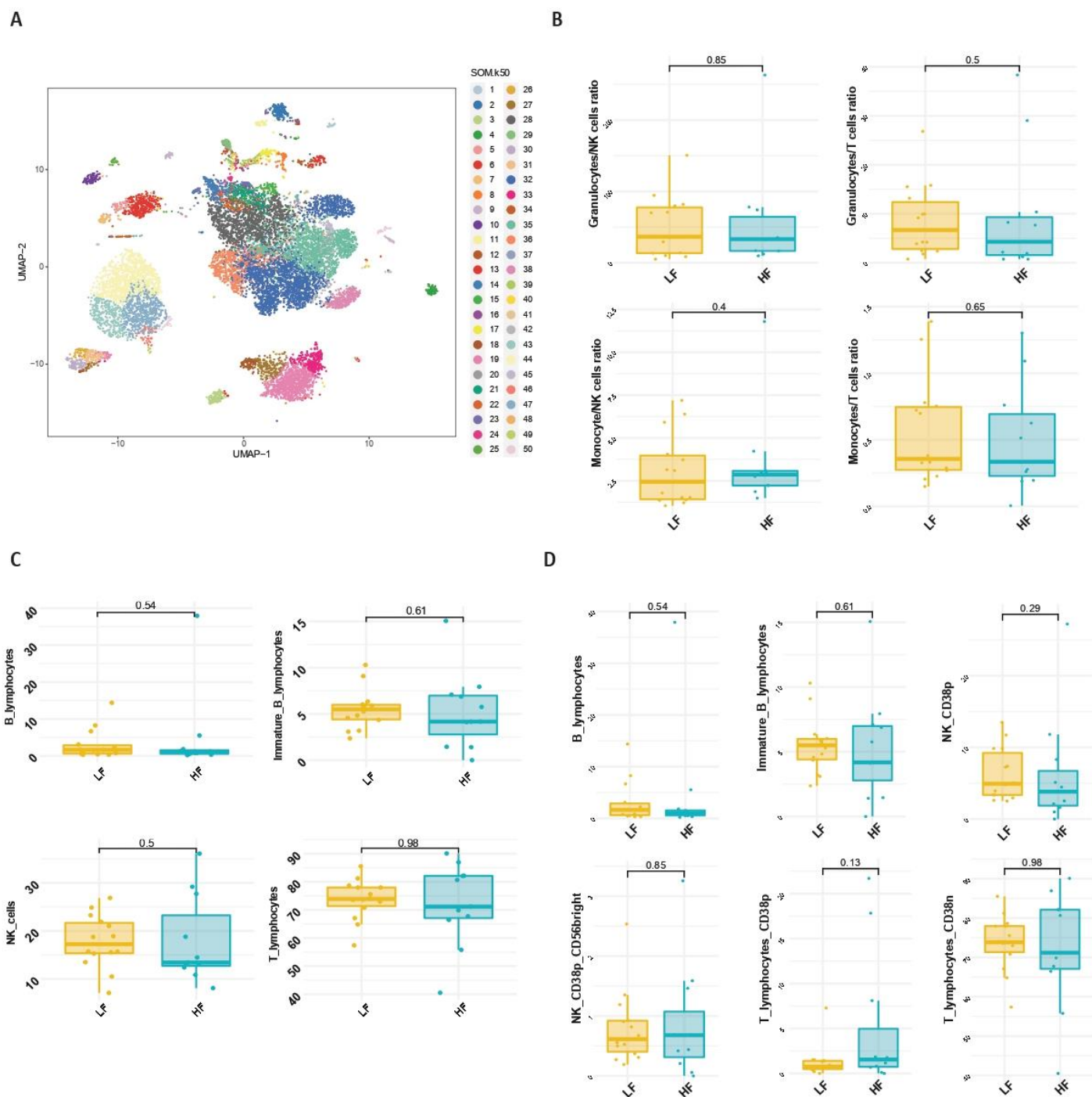


D



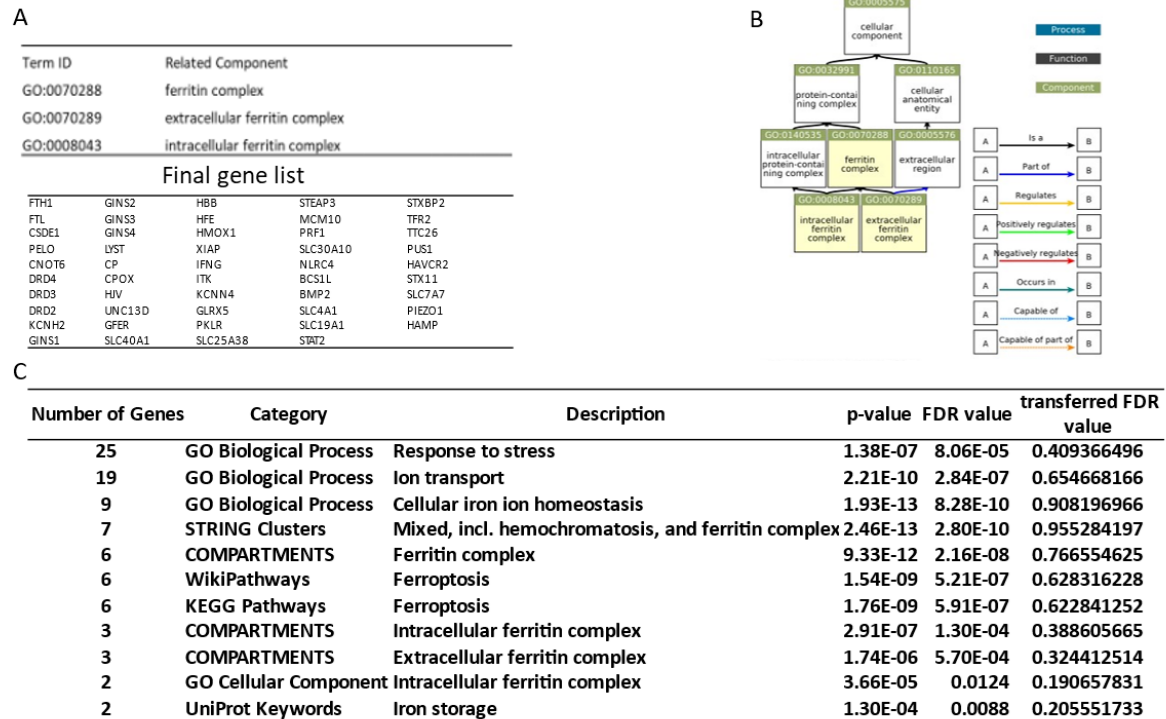
Supplementary Figure S3: FlowCT analysis of BD PCD tube

(A) Uniform manifold approximation and projection (UMAP) of 25 clusters identified by self-organizing map (SOM) of BD OneFlow™ PCD tube. (B) Median expression of individual marker in each cell cluster identified by SOM represented in multi-UMAP plot. (C) Boxplots showed the different frequency of eosinophils, erythroblasts, B and T lymphocytes, and monocytes between low ferritin level group (LF) and high ferritin level group (HF). (D) Boxplots showed the different frequency of T and B lymphocyte subsets between low ferritin level group (LF) and high ferritin level group (HF).

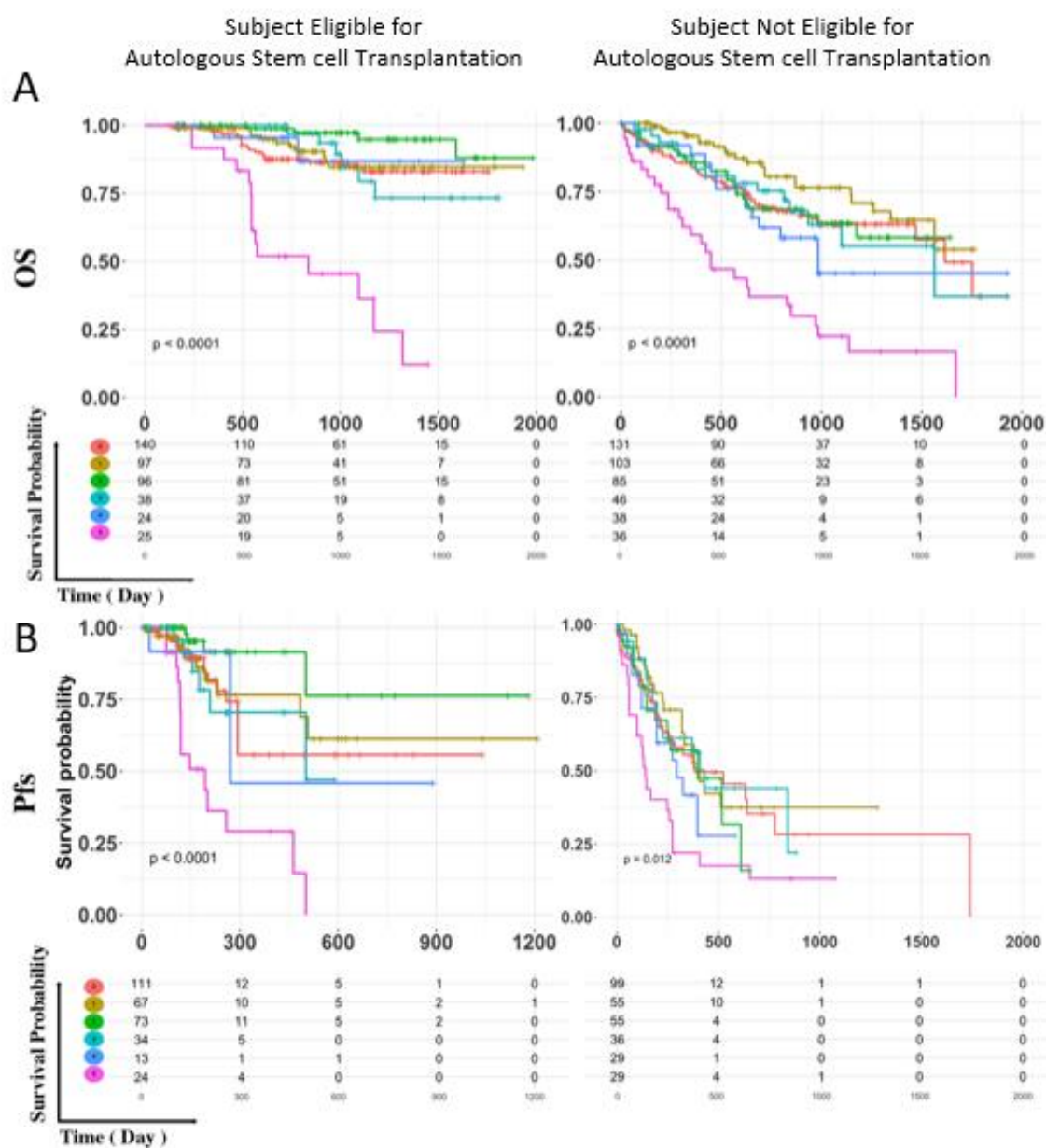


Supplementary Figure S4: FlowCT analysis of PCST tube

(A) Uniform manifold approximation and projection (UMAP) of 50 clusters identified by self-organizing map (SOM) of BD OneFlow™ PCST tube. (B, C) Boxplots showed the different frequency and ratio (with granulocytes and monocytes) of T and B lymphocytes and NK cells between low ferritin level group (LF) and high ferritin level group (HF). (D) Boxplots showed the different frequency of T and B lymphocyte and NK cell subsets between low ferritin level group (LF) and high ferritin level group (HF) after lymphocytes subclustering.

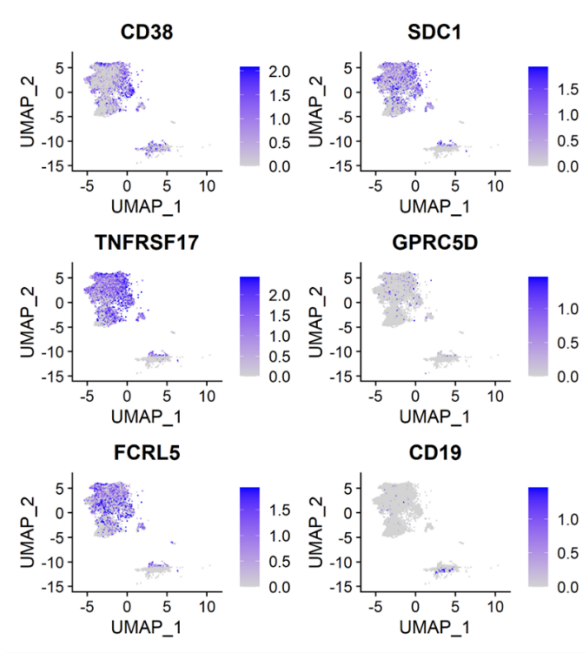


Supplementary Figure S5: a ferritin metabolism-related gene-set that contains 49 genes highly correlated with ferritin biosynthesis : **A**: 3 main gene ontology term was used as a fundamental framework for gene dataset construction. Additionally, we add another dataset from Garcia-Casal MN et al ([PMID:29723227](https://pubmed.ncbi.nlm.nih.gov/29723227/)) from Molecular Signatures Database (MSigDB) to create a dataset that has 49 unique genes. **B**: GO domains network representation. **C**: Enrichment in GO terms from biological processes and KEGG pathways for the identified genes clearly revealed considerable enrichment in ferritin metabolism-related terms, with p-values<0.005 and FDR values< 0.001 regarded as significant enrichment scores.

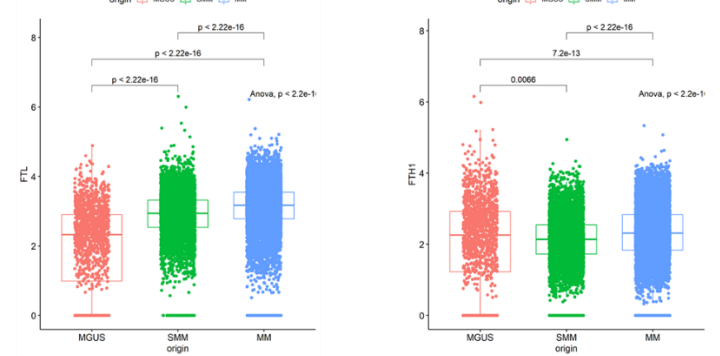


Supplementary Figure S6: Survival analysis of unsupervised patients clusters: based on different ferritin related and/or conserved diverse biological Functions, six different clusters have been identified. Patients were further divided according to their ASCT eligibility: overall survival (OS) and progression free survival (PFS) results were reported in A and B respectively. For both panels, the left picture indicates subjects who are eligible for the ASCT while the right picture subject who are not eligible for ASCT.

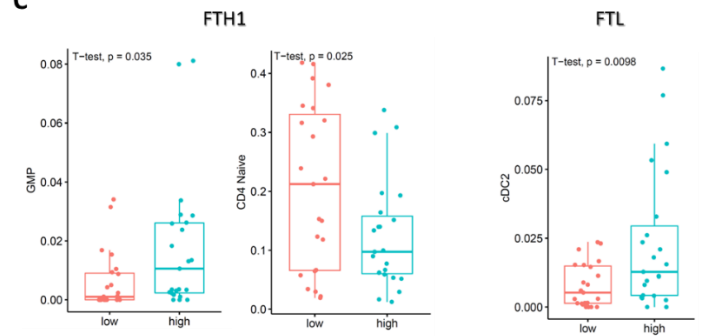
A



B



C



Supplementary Figure S7: single cell RNAseq results: A. gene expression of main markers of plasma cells. B. FTL and FTH1 expression in different conditions and their comparative and overall p.values. C. Additional significant changes in immune populations associated to high or low levels of FTH1/FTL

Supplementary Table S1. Main characteristics of MGUS and SMM patients included in the study

	MGUS (15)	SMM (17)
Sex (M/F)	9/6	8/9
Hb (g/dl)	13.3	12.9
Neutrophils (μL)	4200	4474
Lymphocytes (μL)	2152	1927
Monocytes (μL)	499	482
Platelets (μL)	245333	250725
Creatinin (mg/dL)	0.98	0.86
Albumin (g/L)	6.85	3.97
Calcium (mg/dL)	9.49	9.65
β2M (mg/dL)	2.95	2.68
LDH (U/L)	160	151
Ferritin (ng/ml)	139	116