

Supplementary material

Visual Abstract

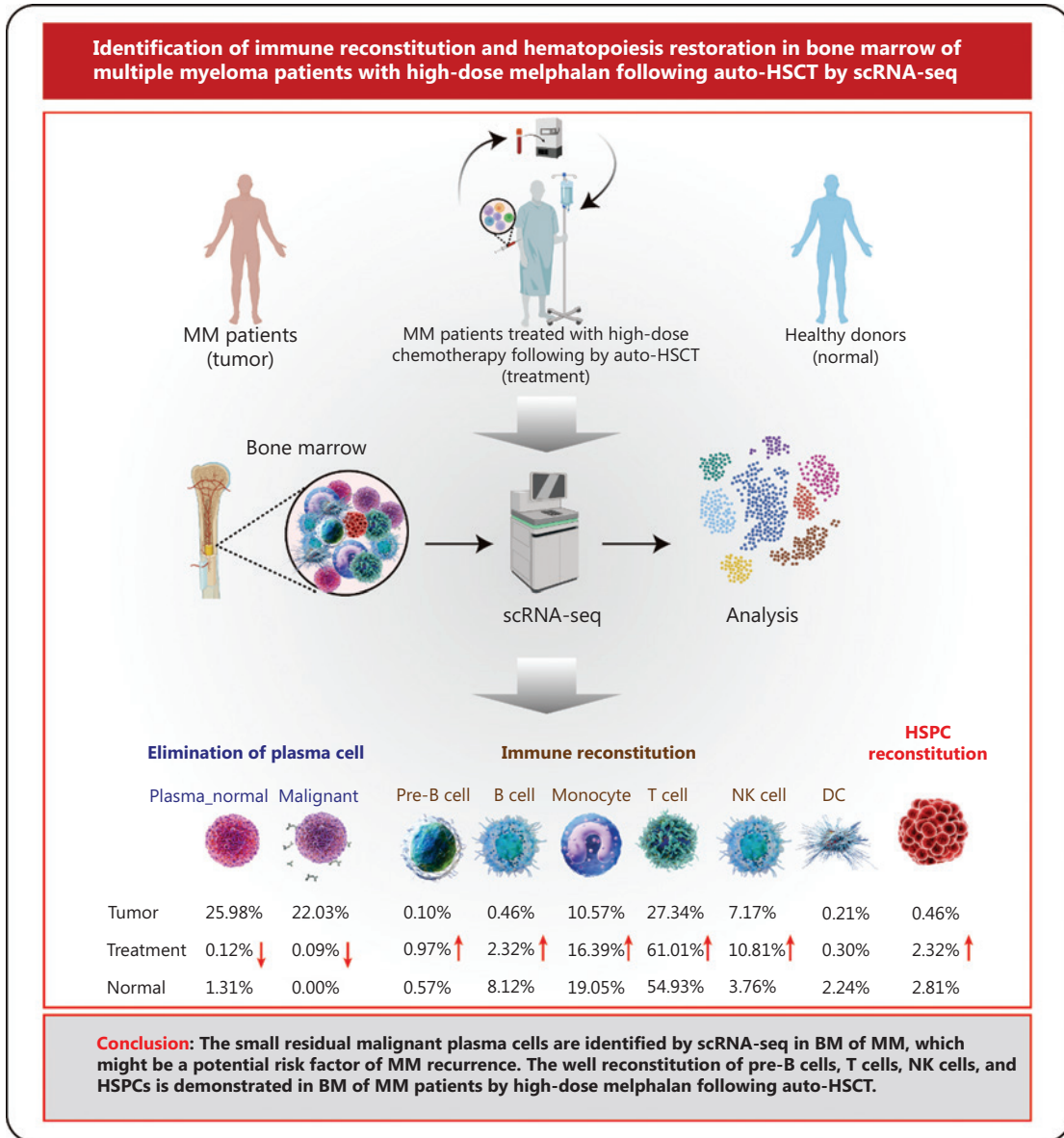


Table S1 Basoc MM patient information

Information	Patients		
	LWG1030	BLW1014	BM0906
Diagnosis date	2023-04-25	2021-12-20	2023-03-01
scRNA sequencing date	2024-10-30	2024-10-14	2024-09-06
Age	55	66	45
Gender	M	F	F
MM type	IgG- κ	IgG- κ	κ light chain
ISS stage	II	II	III
R-ISS	II	II	II
mSMART3.0	High risk	High risk	Standard risk
R2-ISS	Intermediate-high	Intermediate-high	Intermediate-high

ISS, international staging system; R-ISS, revised international staging system.

Table S2 Clinical diagnostic data of MM patients before auto-HSCT

Clinical data	Patients		
	LWG1030	BLW1014	BM0906
Test data	2023-04-25	2021-12-20	2023-03-01
Hemoglobin, g/L	99	96	111
Creatinine, μ mol/L	69	69.2	149
Calcium, mmol/L	2.61	2.41	3.4
Albumin, g/L	22.4	29.8	42.8
B2M, μ g/mL	3	2.35	8.19
LDH, U/L	186	175.7	110
SIFE	IgG- κ	IgG- κ	Negative
SPEP, g/L	69.7	54.1	Negative
UIFE	IgG- κ	Negative	κ light chain
UPEP, g/24 h	2.098	Negative	0.45436
dFLC, mg/L	3,901.47	150.21	2,037.95
BMPCs, %	70	50	67
Bone marrow flow cytometry, %	19.45	7.97	44.92
FISH	1q21+, t (4; 14)	1q21+	Negative

LDH, lactate dehydrogenase; B2M, beta 2 microglobulin; SIFE, serum immunofixation electrophoresis; SPE, serum protein electrophoresis; UPE, urine protein electrophoresis; UIFE, urine immunofixation electrophoresis; dFLC, serum free light chain difference; BMPCs, bone marrow plasma cells; FISH, fluorescence *in situ* hybridization; ND, not done.

Table S3 High-dose chemotherapy following by auto-HSCT for MM patients

Therapy	Patients		
	LWG1030	BLW1014	BM0906
Induction reagent	IRD × 3; DVd × 1	VRD × 4	PAD × 2; KRD × 3;
Mobilization (Date)	2023-09-09 G-CSF + Plerixafor	2022-09-02 CTX + G-CSF; 2023-01-05 G-CSF + Plerixafor	2023-10-20 G-CSF + Plerixafor
Collected MNC (× 10 ⁸ /kg)	14.97	13.42	15.15
Collected CD34 ⁺ (× 10 ⁶ /kg)	10.1	10.6	8.87
Pre-transplant response	VGPR	PR	CR
Conditioning #1 (Date)	2023-09-26 Melphalan 200 mg/m ²	2023-01-29 Melphalan 200 mg/m ²	2023-12-15 Melphalan 200 mg/m ²
Transplant #1 (Date)	2023-09-28 MNC 5.47 × 10 ⁸ /kg; CD34 ⁺ cells 4.07 × 10 ⁶ /kg	2023-01-31 & 2023-02-01 MNC 4.915 × 10 ⁸ /kg; CD34 ⁺ cells 3.61 × 10 ⁶ /kg	2023-12-15 MNC 7.575 × 10 ⁸ /kg; CD34 ⁺ cells 4.435 × 10 ⁶ /kg
Response #1	VGPR	CR	sCR
Conditioning #2 (Date)	2024-02-24 Melphalan 200 mg/m ²	2023-05-17 Melphalan 200 mg/m ²	N/A
Transplant #2 (Date)	2024-02-26 MNC 4.75 × 10 ⁸ /kg; CD34 ⁺ cells 3.03 × 10 ⁶ /kg	2023-05-19 MNC 4.915 × 10 ⁸ /kg; CD34 ⁺ cells 3.61 × 10 ⁶ /kg	N/A
Response #2	sCR	sCR	N/A
Current state	Alive	Alive	Alive
Current response	sCR	sCR	sCR

IRD, ixazomib, lenalidomide, dexamethasone; DVd, daratumumab, bortezomib, dexamethasone; VRD, bortezomib, lenalidomide, dexamethasone; PAD, bortezomib, doxorubicin, dexamethasone; KRD, carfilzomib, lenalidomide, dexamethasone; G-CSF, granulocyte colony-stimulating factor; CTX, cyclophosphamide; MNC, mononuclear cell; MR, minimal response; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response. Response was assessed according to the IMWG consensus.

Table S4 Clinical diagnostic data of MM patients after auto-HSCT during follow-up evaluations

Clinical data	Patients		
	LWG1030	BLW1014	BM0906
Follow-up time (months)	26	41	27
Hemoglobin, g/L	114	117	137
Creatinine, $\mu\text{mol/L}$	71	96	56
Calcium, mmol/L	2.21	2.05	2.31
Albumin, g/L	47.7	39.2	46.9
B2M, $\mu\text{g/mL}$	2.01	2.35	2.28
LDH, U/L	138	161	192
SIFE	Negative	Negative	Negative
SPEP, g/L	Negative	Negative	Negative
UIFE	Negative	Negative	κ light chain
UPEP, g/24 h	Negative	Negative	Negative
dFLC, mg/L	Negative	Negative	Negative
BMPCs, %	Negative	Negative	Negative
Bone marrow flow cytometry, %	Negative	Negative	Negative
FISH	ND	ND	ND

LDH, lactate dehydrogenase; B2M, beta 2 microglobulin; SIFE, serum immunofixation electrophoresis; SPE, serum protein electrophoresis; UPE, urine protein electrophoresis; UIFE, urine immunofixation electrophoresis; dFLC, serum free light chain difference; BMPCs, bone marrow plasma cells; FISH, fluorescence *in situ* hybridization; ND, not done.

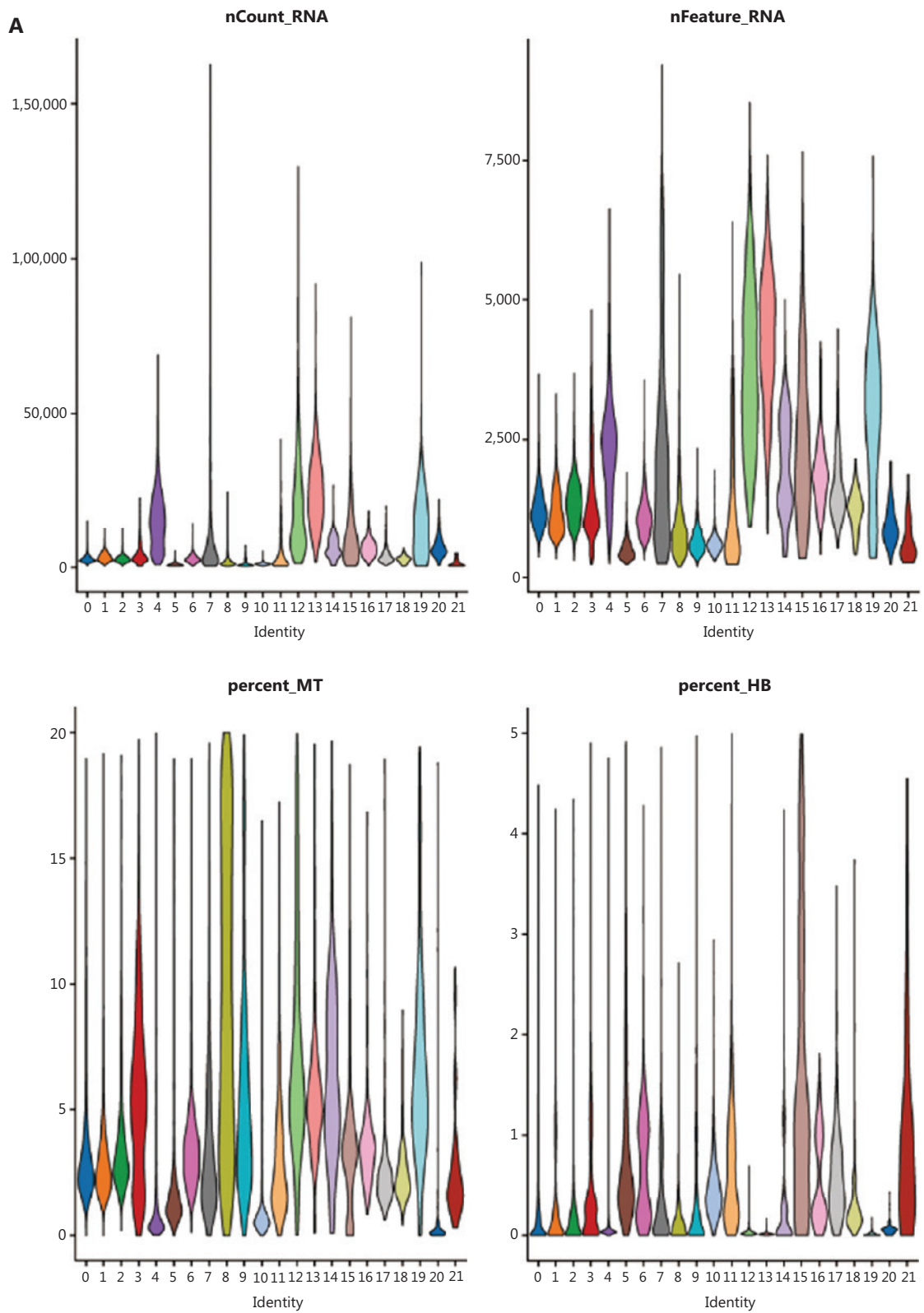


Figure S1 Continued

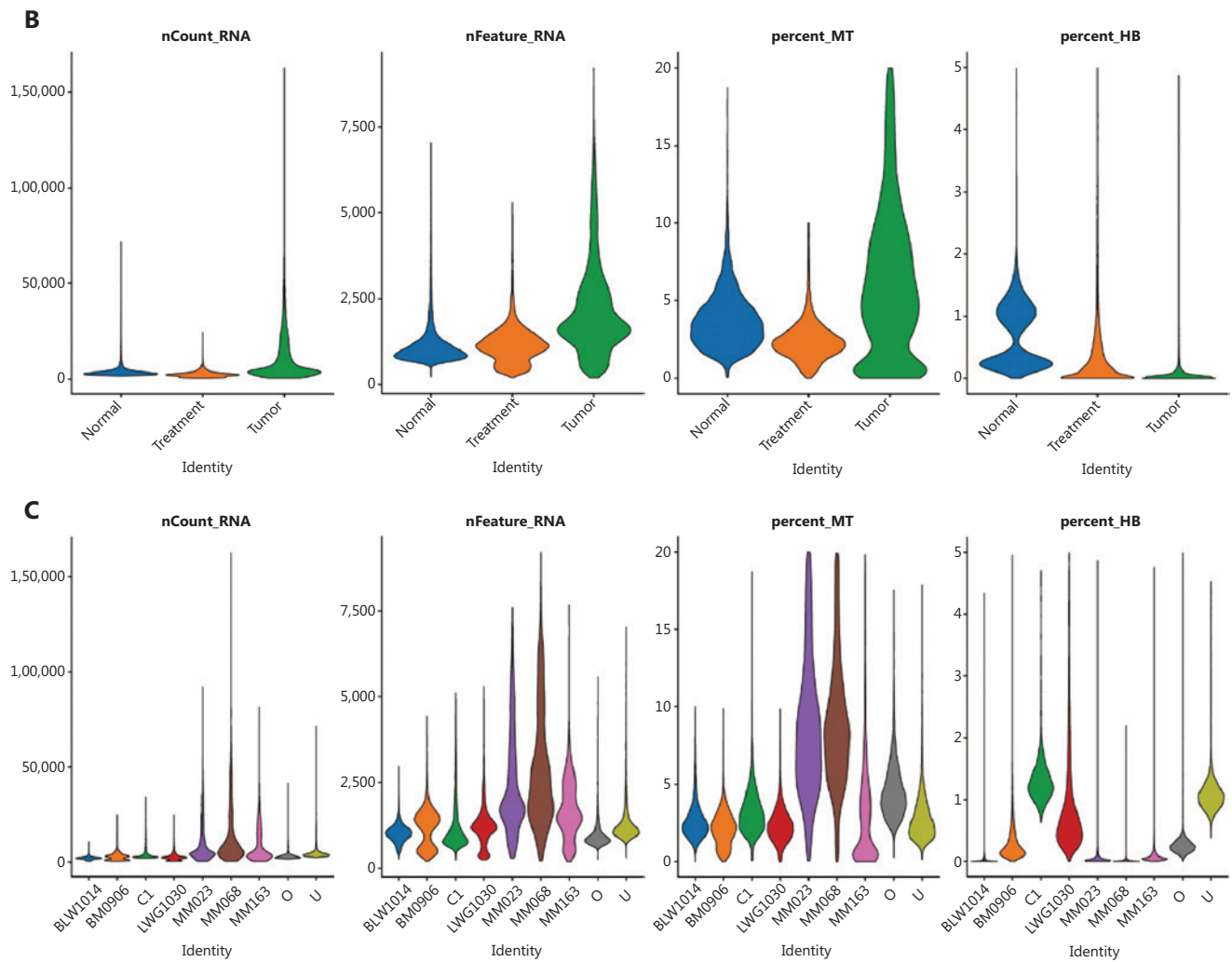


Figure S1 The quality control of single-cell transcriptomic profiling of bone marrow mononuclear cells. The violin plot of the cell count, feature count, mitochondrial gene ratio, and red blood cell gene ratio for clustering (A), grouping (B), and sampling (C). The y-axis represents gene numbers in each cell. MT, mitochondrial; HB, hemoglobin.

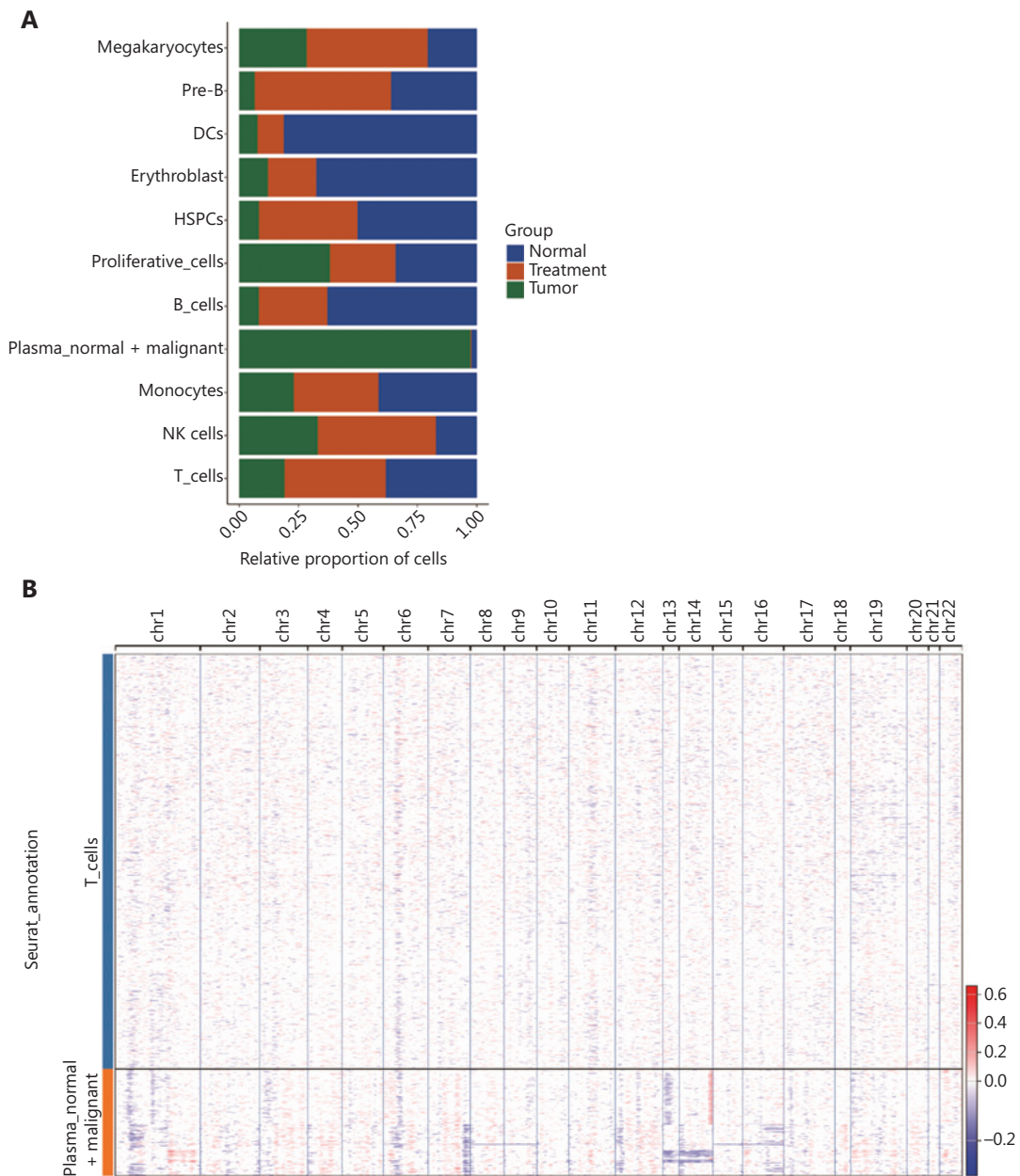


Figure S2 Transcriptional remodeling of plasma cells following BM of MM patients by the therapy. (A) Stacked bar chart comparing the relative abundance of cell types across the three groups. (B) Recognition of malignant plasma cells across the three groups. Malignant and non-malignant cells in plasma B cells were identified with default parameters using the Infercnvpy package, in which T cells were used as normal controls. The heatmap shows the copy number changes with red colors indicating a significant increase in copy number (amplification/gain) and blue colors indicating a significant decrease in copy number (deletion/loss). DCs, dendritic cells; HSPCs, hematopoietic stem and progenitor cells.

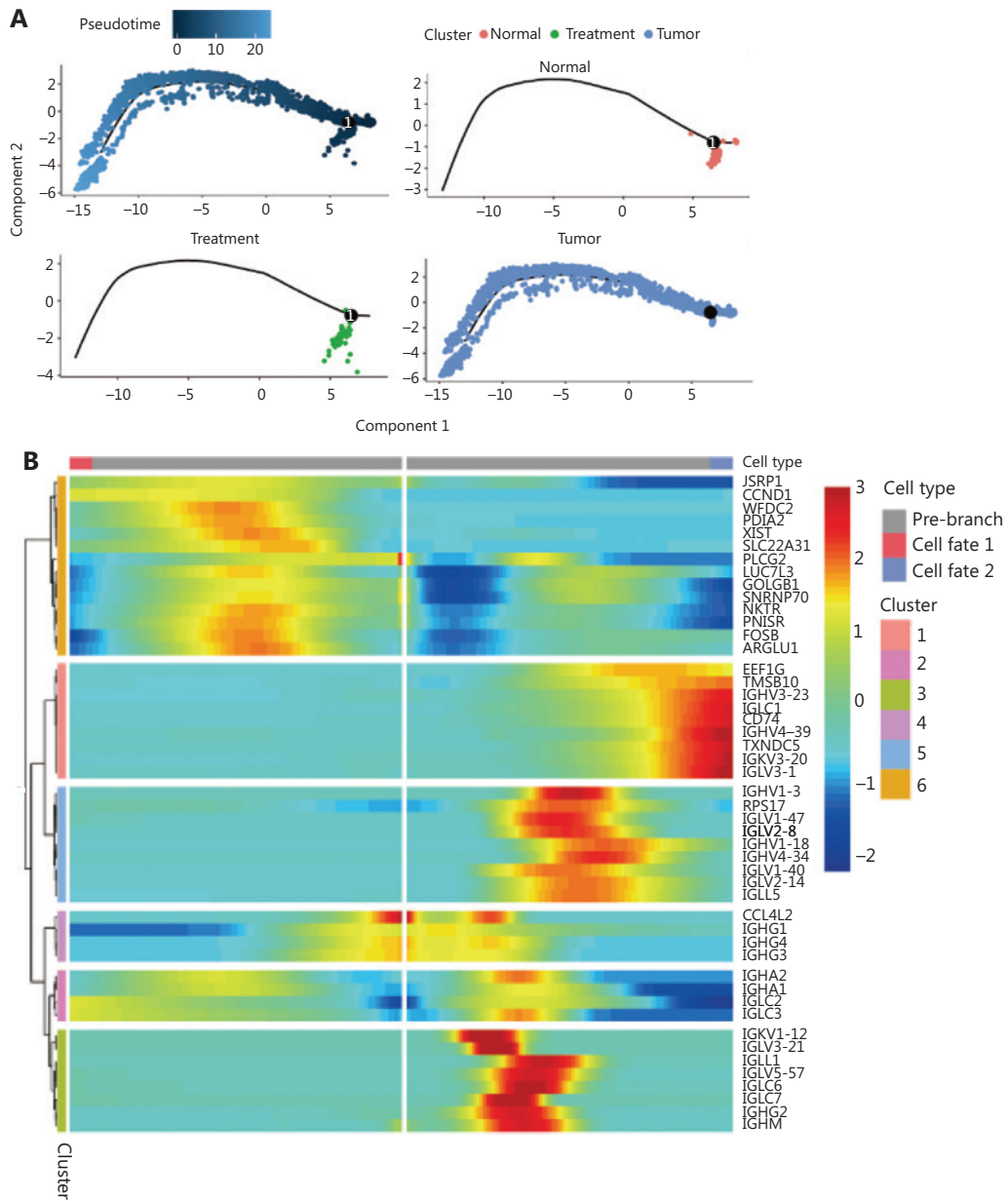


Figure S3 Continued

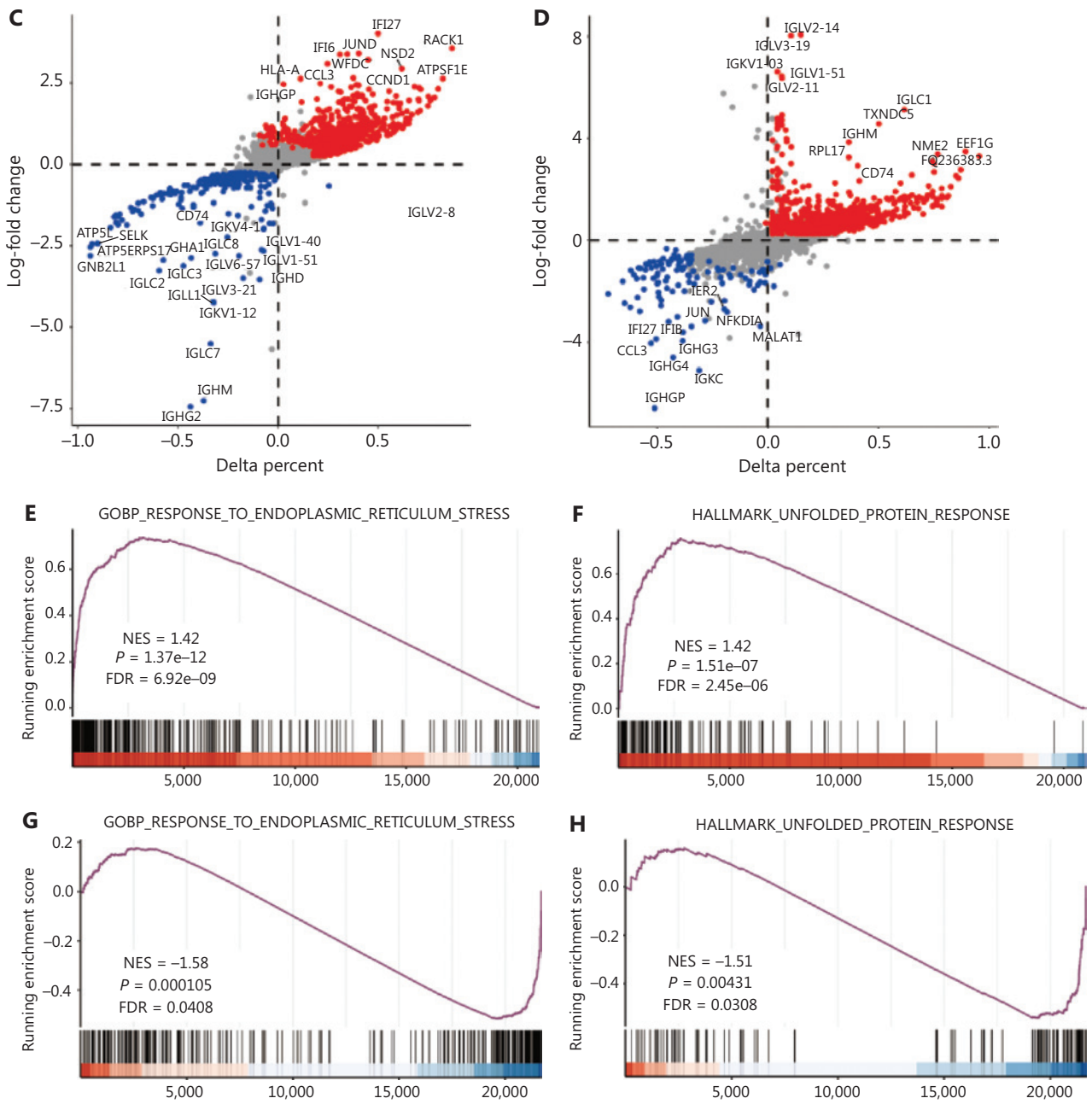


Figure S3 Continued

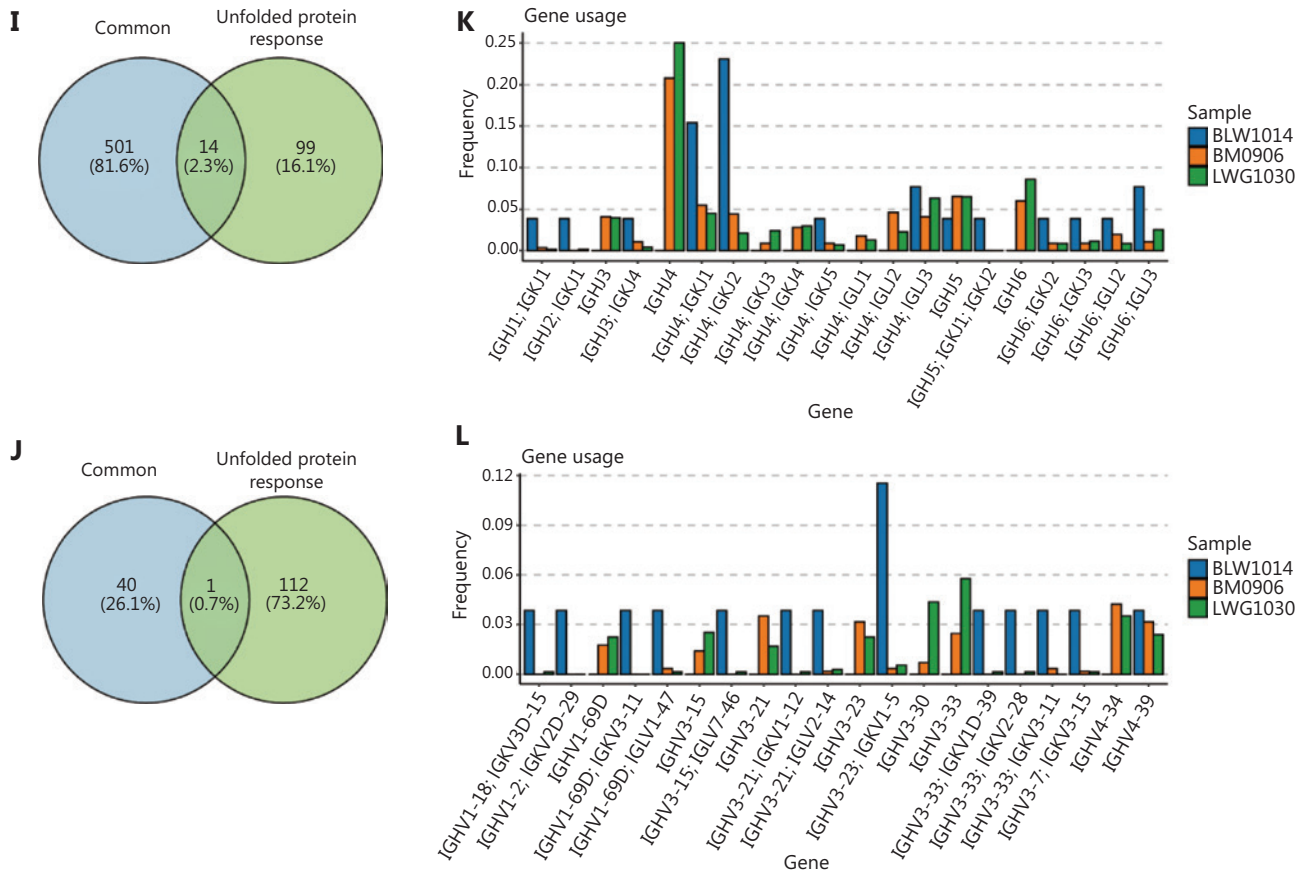


Figure S3 Identification of transcriptional remodeling of plasma cells in the BM of MM patients by therapy. (A) Pseudotime trajectory of plasma cells inferred by Monocle 2, colored by pseudotime score, and the distribution of plasma cells from HD (for normal), MM (for tumor), and auto-HSCT samples (for treatment) along the pseudotime trajectory inferred by monocle 2. (B) Heatmap of the top 50 differentially expressed genes across plasma cell trajectory states. (C–H) Volcano plots of DEGs between MM vs. HD (C) and auto-HSCT vs. MM (D) plasma cells. GSEA GO (E) and HALLMARK (F) analysis of DEGs between MM vs. HD. GSEA GO (G) and HALLMARK (H) analysis of DEGs between auto-HSCT vs. MM. (I) Overlap analysis identifying 14 Unfolded Protein Response (UPR)-related genes from the 515 gene set. (J) Overlap analysis identifying 1 UPR-related genes from the 41 gene set. (K, L) Histogram plot of the frequency of use of the top 20 groups in IGHJ (K) and IGHV (L). GSEA, gene set enrichment analysis; GO, gene ontology; DEGs, differential expressed genes; IGHV, immunoglobulin heavy chain variable region; IGHJ, immunoglobulin heavy chain joining region.

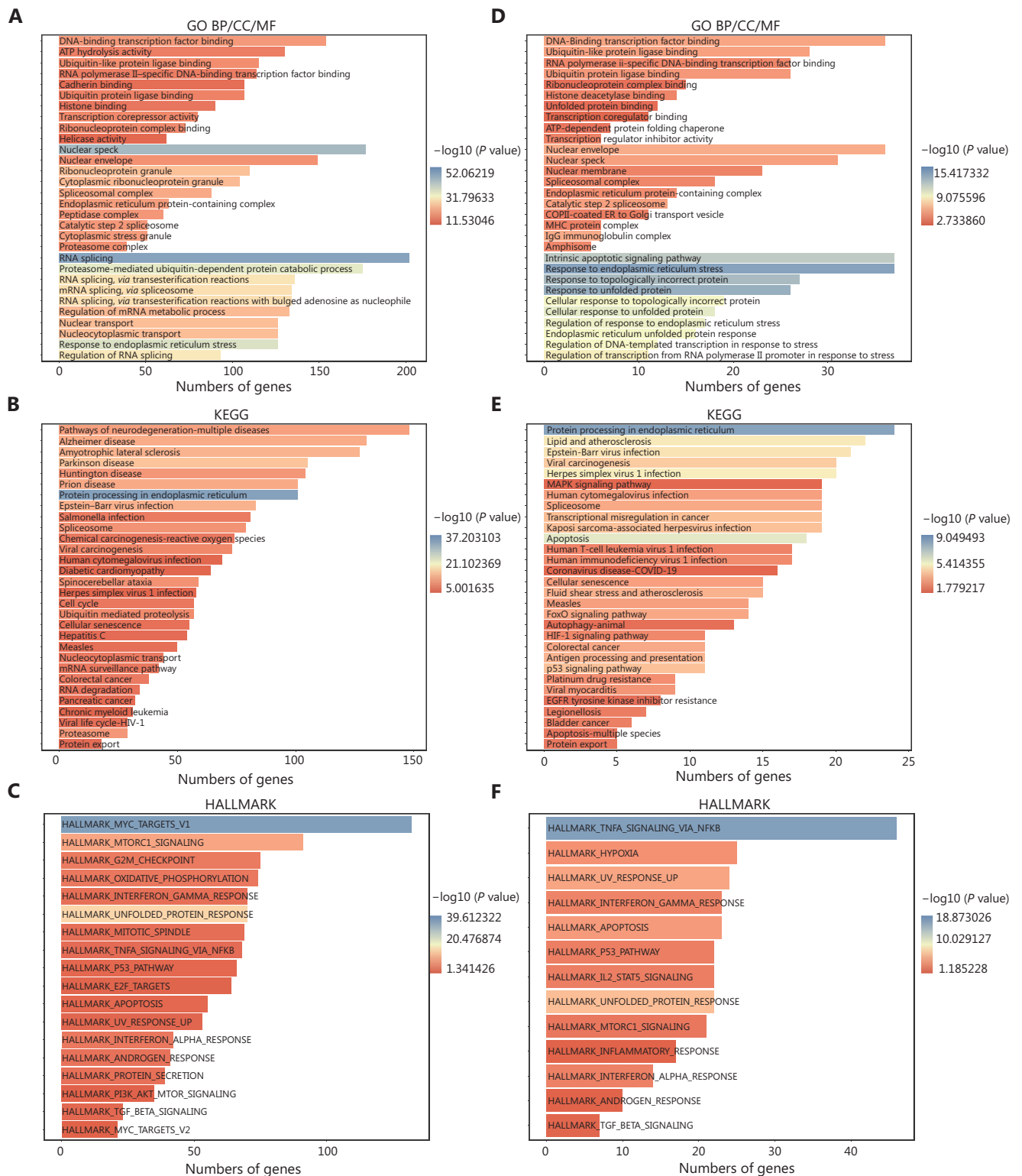


Figure S4 Functional enrichment of upregulated DEGs in the BM of MM patients by therapy. (A) The bar plot of GO enrichment differences between the MM (for tumor) and HD (for normal) groups. (B) The bar plot of KEGG enrichment differences between the tumor and normal groups. (C) The bar plot of HALLMARK enrichment differences between the tumor and normal groups. (D) The bar plot of GO enrichment

differences between the MM and auto-HSCT groups. (E) The bar plot of KEGG enrichment differences between the MM and auto-HSCT groups. (F) The bar plot of HALLMARK enrichment differences between the MM and auto-HSCT groups. GO, gene ontology; BP, biological process; CC, cellular component; MF, molecular function; KEGG, Kyoto encyclopedia of genes and genomes.

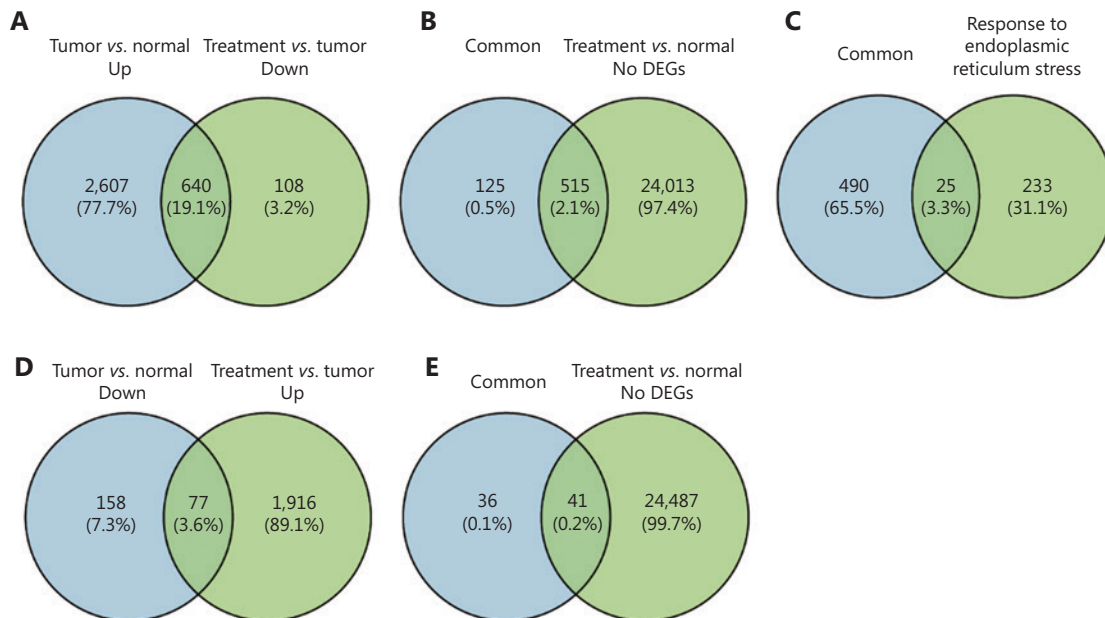


Figure S5 Transcriptional remodeling of plasma cells in the BM of MM patients by therapy. (A) Venn diagram of intersecting DEGs between MM (for tumor) vs. HD (for normal) upregulated genes and auto-HSCT (for treatment) vs. MM downregulated genes ($n = 640$). (B) Venn diagram shows 515 of these genes are not significantly different between auto-HSCT and HD. (C) Overlap analysis identifying 25 endoplasmic reticulum (ER) stress-related genes from the 515 gene set. (D) Venn diagram of intersecting DEGs between MM vs. HD downregulated genes and auto-HSCT vs. MM upregulated genes ($n = 77$). (E) Venn diagram shows 41 of these genes are not significantly different between auto-HSCT and HD. DEGs, differentially expressed genes.