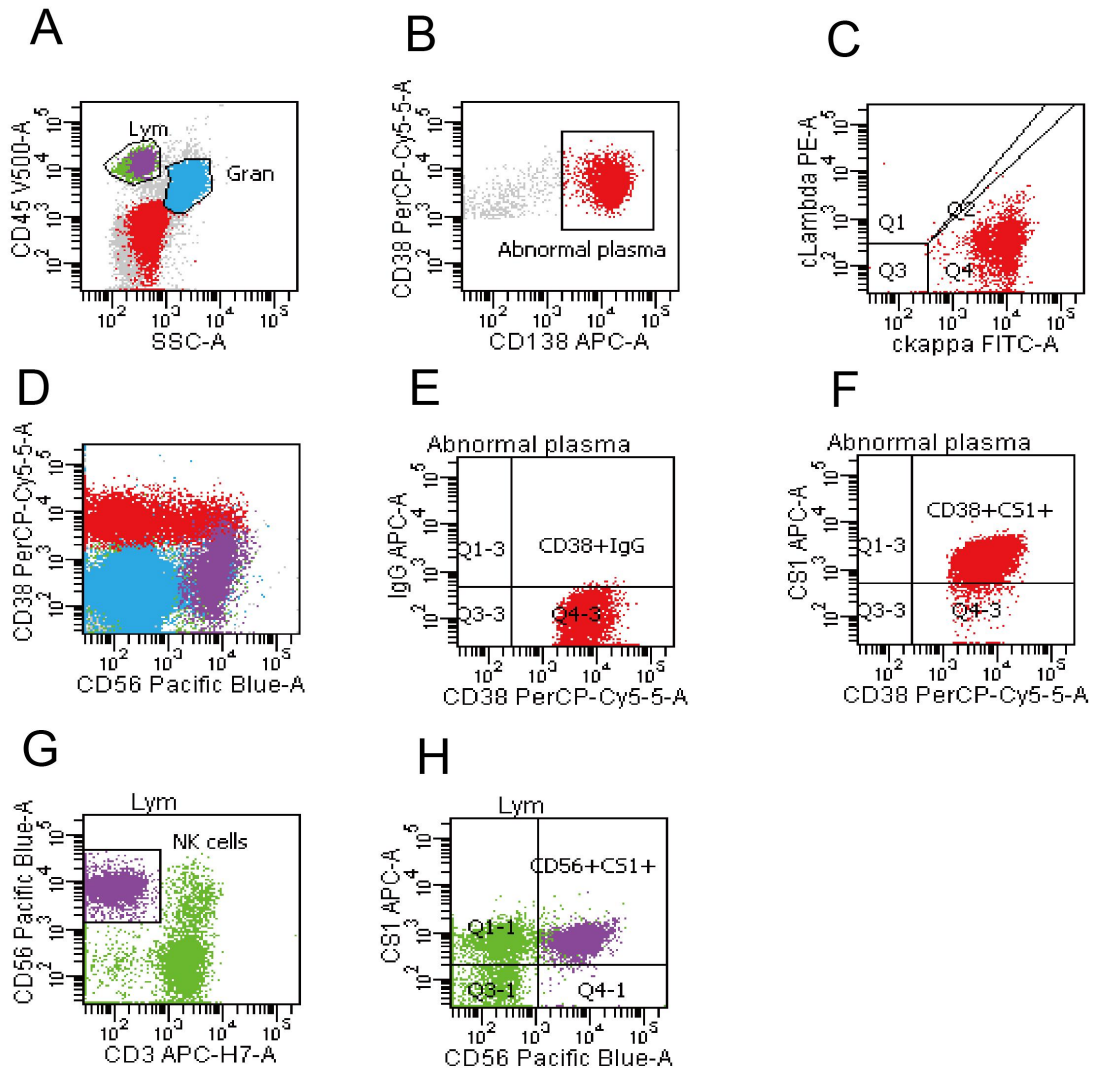1   **Supplementary Material**

2   **Supplemental Figures**

Figure S1

3

4   **Figure S1. The detailed gated method of flow cytometry.**
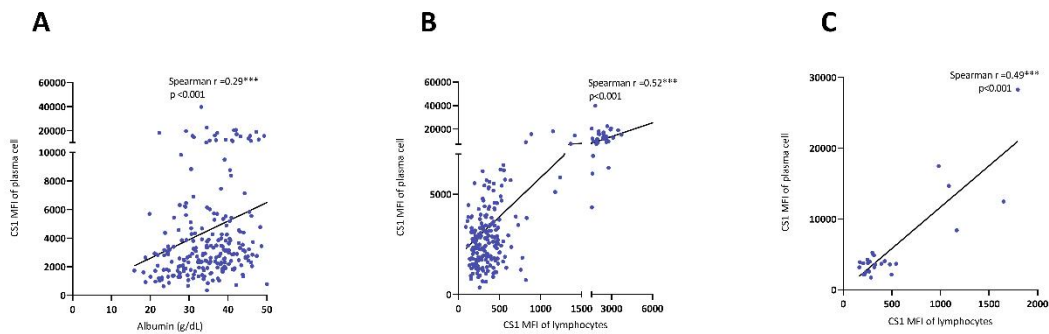
5   (A) The lymphocytes and granulocytes were gated by CD45 and SSC. (B-E)

6   SSC/CD38/CD45 /CD138 /CD56, as well as ckappa and clambdas were used to gate the

1 abnormal plasma cells. (F) CS1 expression in these abnormal plasma cells (G-H) Within the

2 lymphocyte gate, the NK cell population were gated by CD3$^-$/CD56$^+$, and then CS1

3 expression was analyzed in them.

4

Figure S2

5

6 **Figure S2. Spearman correlation analysis of CS1 expression of plasma cells and clinical**

7 **parameters.** (A)displayed Spearman relationships between serum albumin concentration
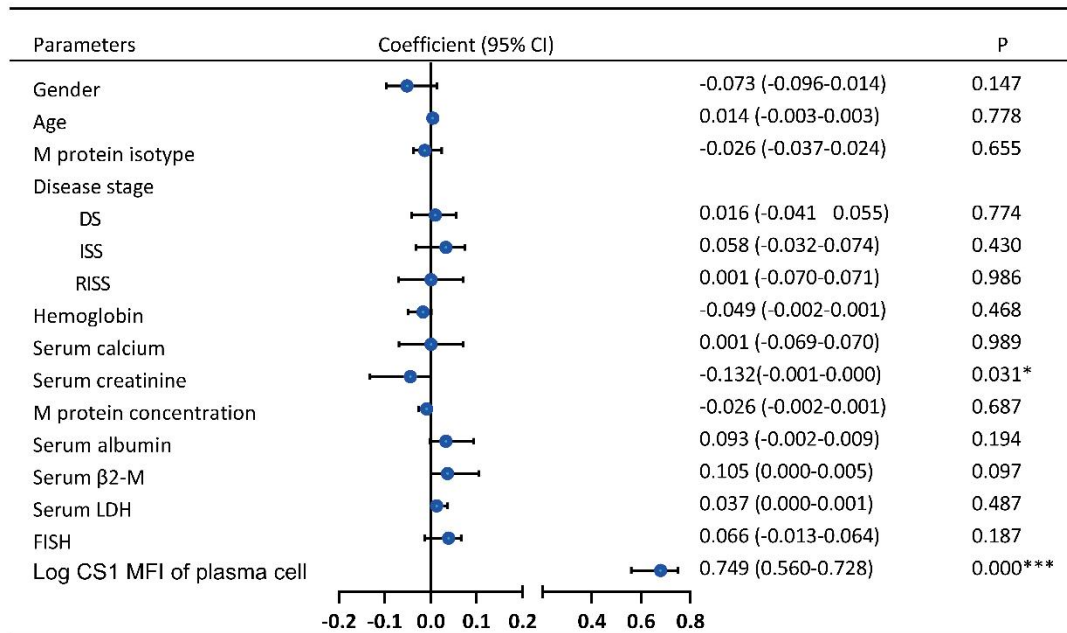
8 and the CS1 MFI of plasma cells in MM. (B) and (C) displayed Spearman correlations

9 between the CS1 MFI of lymphocytes and the CS1 MFI of plasma cells in MM and other

10 PCDs respectively. ***:P<0.001.

11

Figure S3

| Parameters	Coefficient (95% CI)		P
Gender		-0.073 (-0.096-0.014)	0.147
Age		0.014 (-0.003-0.003)	0.778
M protein isotype		-0.026 (-0.037-0.024)	0.655
Disease stage			
DS		0.016 (-0.041 0.055)	0.774
ISS		0.058 (-0.032-0.074)	0.430
RISS		0.001 (-0.070-0.071)	0.986
Hemoglobin		-0.049 (-0.002-0.001)	0.468
Serum calcium		0.001 (-0.069-0.070)	0.989
Serum creatinine		-0.132(-0.001-0.000)	0.031*
M protein concentration		-0.026 (-0.002-0.001)	0.687
Serum albumin		0.093 (-0.002-0.009)	0.194
Serum β2-M		0.105 (0.000-0.005)	0.097
Serum LDH		0.037 (0.000-0.001)	0.487
FISH		0.066 (-0.013-0.064)	0.187
Log CS1 MFI of plasma cell		0.749 (0.560-0.728)	0.000***

-0.2 -0.1 0.0 0.1 0.2   0.4 0.6 0.8

1

Figure S3. Multivariate Analysis for the CS1 expression of plasma cell in MM.

The forest plot shows the correlation between CS1 expression levels of plasma cells and clinical parameters through multivariate linear regression analysis. The expression level of CS1 in NK cells is independently associated with the expression level of CS1 in clonal plasma cells.
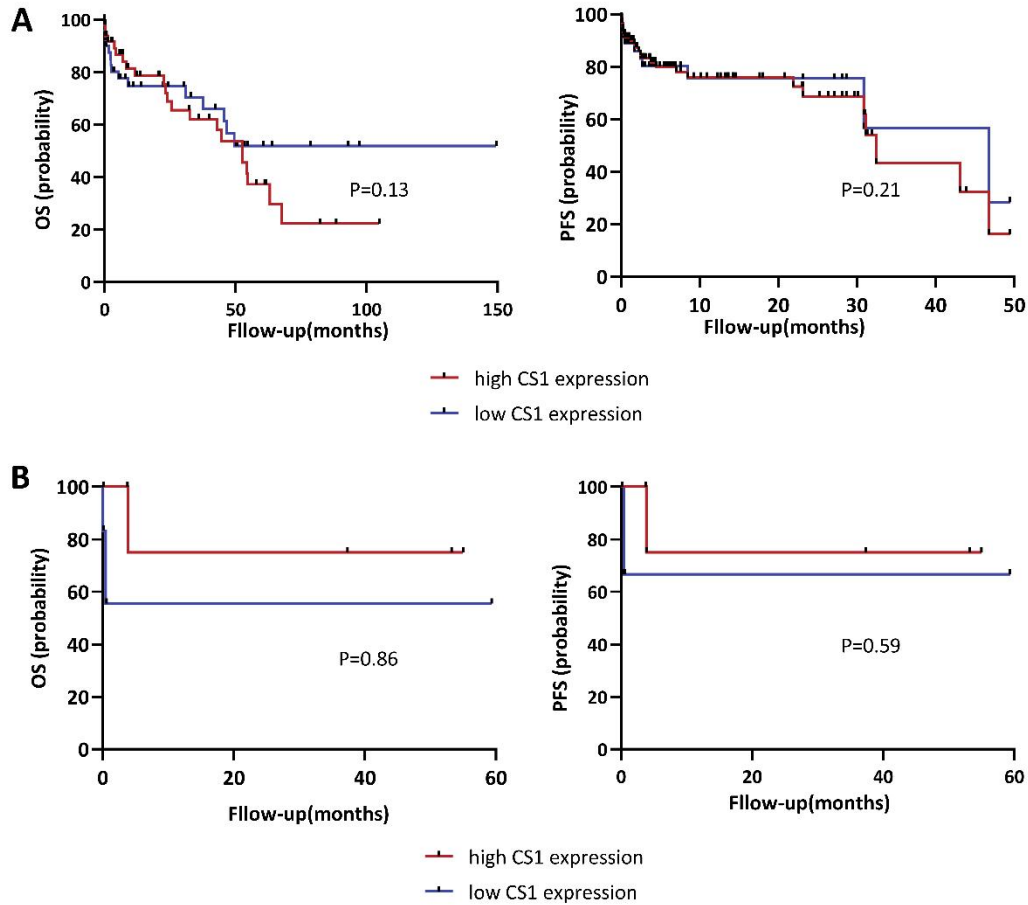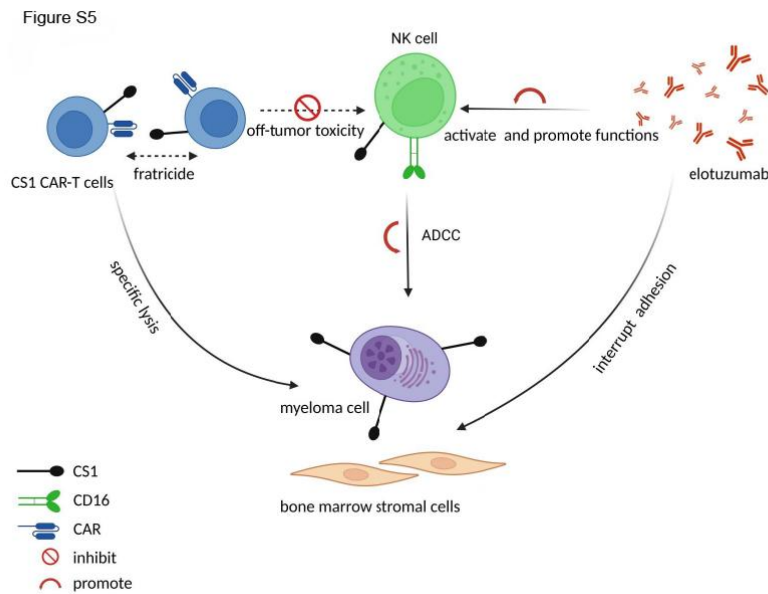
Figure S4

Figure S4. The correlation of CS1 expression level of plasma cells with PFS, OS.

(A-B) Comparative analysis the OS and PFS between patients with high and low CS1 expression of plasma cells in MM and other PCDs respectively. According to the expression of CS1 on monoclonal plasma cells, patients were divided into a high expression group (CS1 MFI ≥ the 75th percentile) and a low expression group (CS1 MFI ≤ the 25th percentile).

1

2

Figure S5. Expression of CS1 on NK cells has implications for immunotherapy targeting CS1. Elotuzumab relies on NK cells to induce myeloma cell lysis through ADCC and may also disrupt adhesion between myeloma cells and bone marrow stromal cells. Therefore, selecting a less pretreated patient and increasing the number and function of NK cells may be the convincible ways to promote the efficacy of Elotuzumab. Killing NK cells by CS1 CAR-T not only leads to excessive toxicity but also weakens the immunological effect of NK cells against MM. Therefore, avoiding killing NK cells by CS1 CAR-T helps improve safety and efficacy. This figure was created with BioRender.com.

1   **Supplementary Tables**

2

	OS		PFS	
	HR (95%CI)	*P*	HR (95%CI)	*P*
Sex	0.769(0.502-1.178)	0.227	0.954(0.668-1.362)	0.794
Age	1.032(1.009-1.055)	0.006**	1.019(1.001-1.038)	0.041*
DS Stage 3	1.074(0.605-1.907)	0.808	0.748(0.446-1.254)	0.271
ISS Stage 3	1.405(0.799-2.469)	0.237	1.208(0.748-1.95)	0.440
RISS Stage 3	0.607(0.305-1.208)	0.155	0.889(0.5-1.58)	0.688
Hemoglobin	0.995(0.984-1.005)	0.314	0.994(0.985-1.003)	0.180
Calcium	1.901(1.085-3.331)	0.025*	1.368(0.875-2.139)	0.169
Creatinine	1(0.999-1.002)	0.867	1(0.999-1.001)	0.856
M protein	0.997(0.987-1.007)	0.539	1.001(0.992-1.01)	0.822
Albumin	0.988(0.946-1.031)	0.571	0.999(0.963-1.036)	0.966
β2-M	1.018(0.999-1.038)	0.070	1.026(1.008-1.044)	0.004**
LDH	1.001(1-1.001)	0.208	1(0.999-1.001)	0.693
High Risk genetic Abnormalities	1.015(0.633-1.627)	0.951	0.976(0.650-1.464)	0.905
Bone marrow plasma cells	0.998(0.985-1.012)	0.796	1.006(0.994-1.018)	0.347
CS1 MFI of natural killer cells	1(1-1.001)	0.253	1(1-1.001)	0.102
CS1 MFI of plasma cells	1(0.999-1)	0.221	0.999(0.999-1)	0.172

3   **Table S1. Cox multivariate analysis of PFS and OS in multiple myeloma patients**

4   Abbreviations: ISS, Internal Staging System; R-ISS, Revised ISS; DS, Durie-Salmon; M Protein, Monoclonal protein; β2-M, β2-microglobulin;

5   LDH, lactic dehydrogenase; MFI, mean fluorescence intensity; *: *p* values less than 0.05 (two-tailed) were considered statistically significant; **:

6   *P<0.01*