

Supplemental Content

Table S1. Association of Siglec-15 and PD-L1 Expression With Clinical Characteristics in the Validation Cohort

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44 **Table S1. Association of Siglec-15 and PD-L1 Expression With Clinical**
 45 **Characteristics in the Validation Cohort**

Characteristic	Total (n = 50), %	Siglec-15		<i>p</i> Value	PD-L1		<i>p</i> Value
		Negative	Positive		Negative	Positive	
Age(years)							
<60	15(30.00)	13	2	0.18	8	7	0.5
≥60	35(70.00)	24	11		15	20	
Gender							
Male	27(54.00)	20	7	0.99	11	16	0.42
Female	23(46.00)	17	6		12	11	
Clinical stage							
I	38(76.00)	29	9	0.25	19	19	0.25
II	9(18.00)	7	2		2	7	
IIIa	3(6.00)	1	2		2	1	
T classification							
T1	18(36.00)	13	5	0.36	11	7	0.16
T2	22(44.00)	17	5		9	13	
T3	7(14.00)	6	1		1	6	
T4	3(6.00)	1	2		2	1	

p* < 0.05, *p* < 0.01 and ****p* < 0.001.

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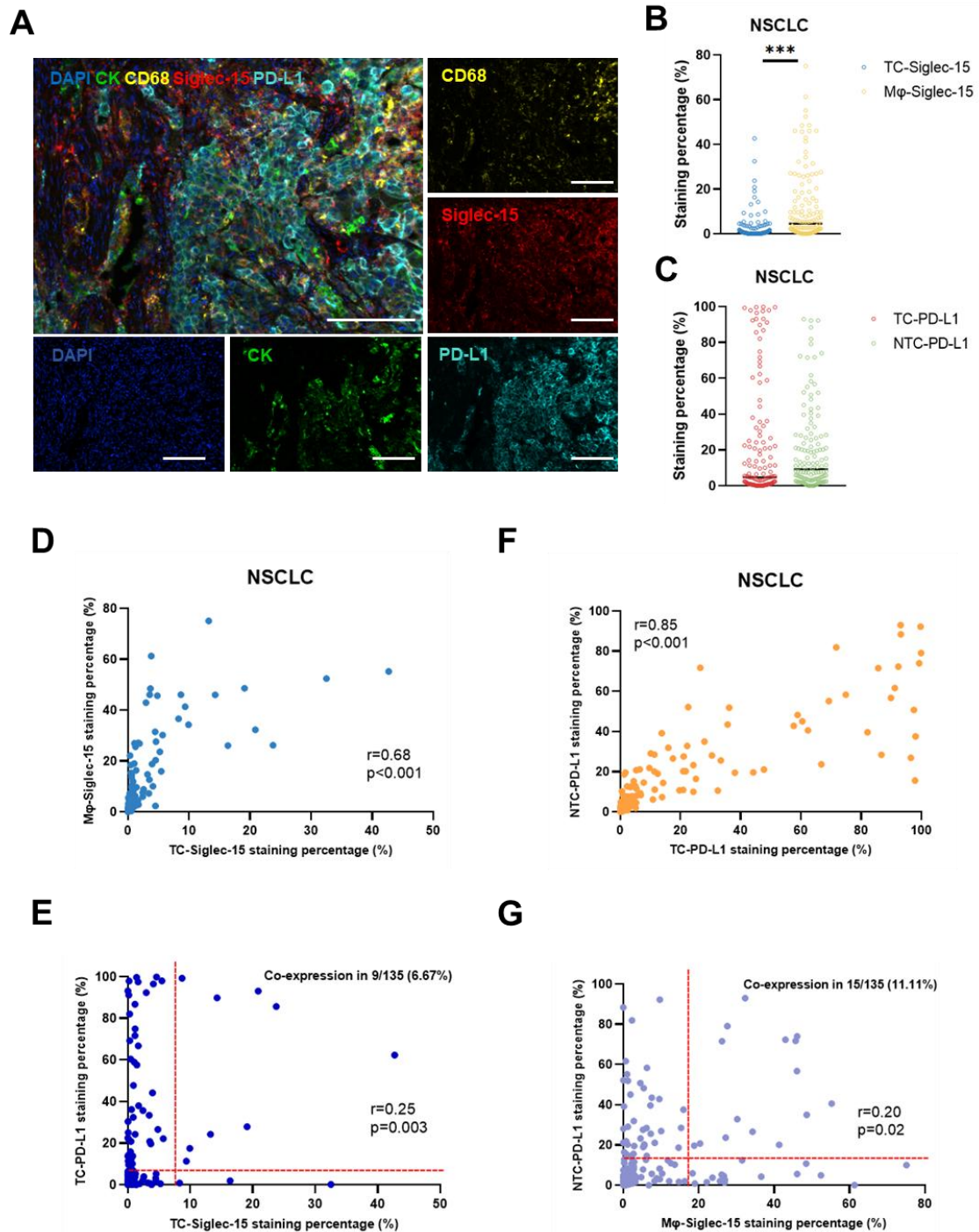


Fig. S1. Siglec-15 and PD-L1 expression in NSCLC tissues.

(A) Representative images of NSCLC tissue section with multiplex immunofluorescence staining with the indicated markers. Scale bar, 50 μ m. (B) Analysis of the percentages of Siglec-15 staining NSCLC tumor cells and macrophages. Tumor cells were identified as pan-cytokeratin positive, and macrophages were identified as CD68 positive. The bar indicates mean. (C) Analysis of the percentages of PD-L1 staining NSCLC tumor cells and non-tumor cells. Tumor cells were identified as pan-cytokeratin positive, and non-tumor cells were identified as pan-cytokeratin negative. The bar indicates mean. (D) Correlation between TC-

Siglec-15 and Mφ-Siglec-15 staining percentages on the same tumor sections. (E) The co-expression and correlation between TC-Siglec-15 staining percentage and TC-PD-L1 staining percentage on the same tumor sections. (F) Correlation between TC-PD-L1 and NTC-PD-L1 staining percentages on the same tumor sections. (G) The co-expression and correlation between Mφ-Siglec-15 staining percentage and NTC-PD-L1 staining percentage on the same tumor sections. * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$; Correlation calculations represent Pearson's coefficient.

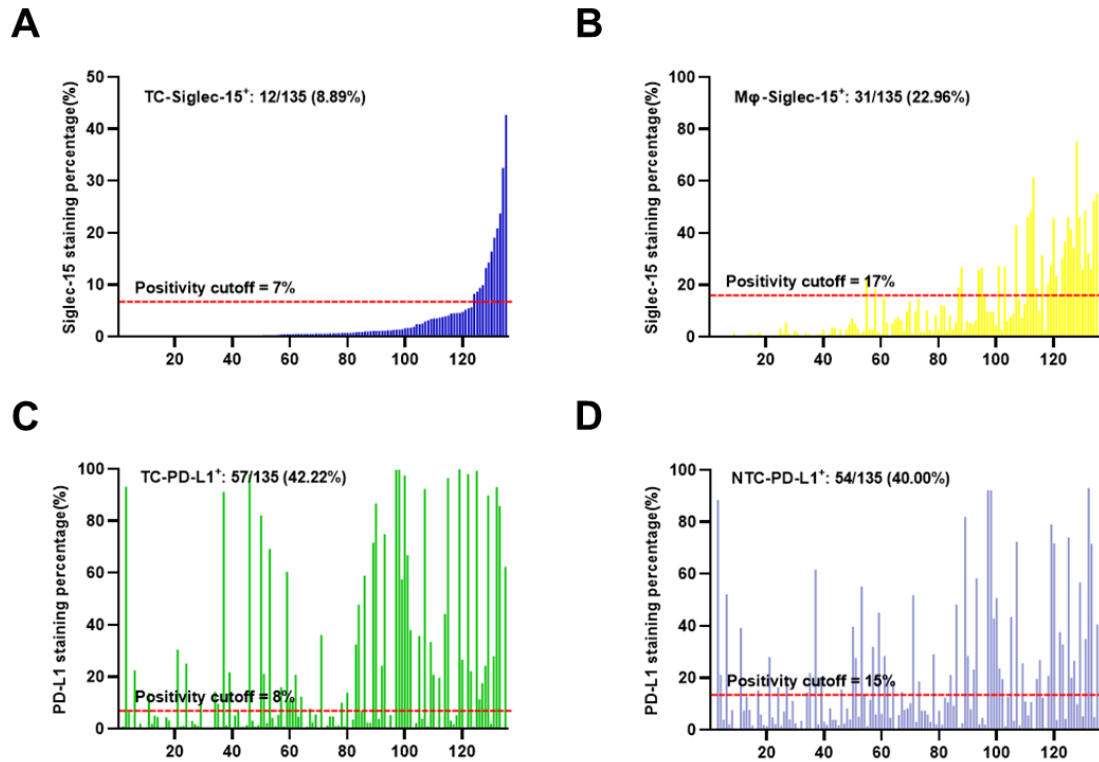


Fig. S2. Staining percentage of Siglec-15 and PD-L1 in NSCLC tissues.
 (A-D) Distribution of TC-Siglec-15 (A), Mφ-Siglec-15 (B), TC-PD-L1 (C) and NTC-PD-L1 (D) staining percentage in the primary NSCLC cohort. Numbers and percentage of patient cases with positive Siglec-15 staining are shown.

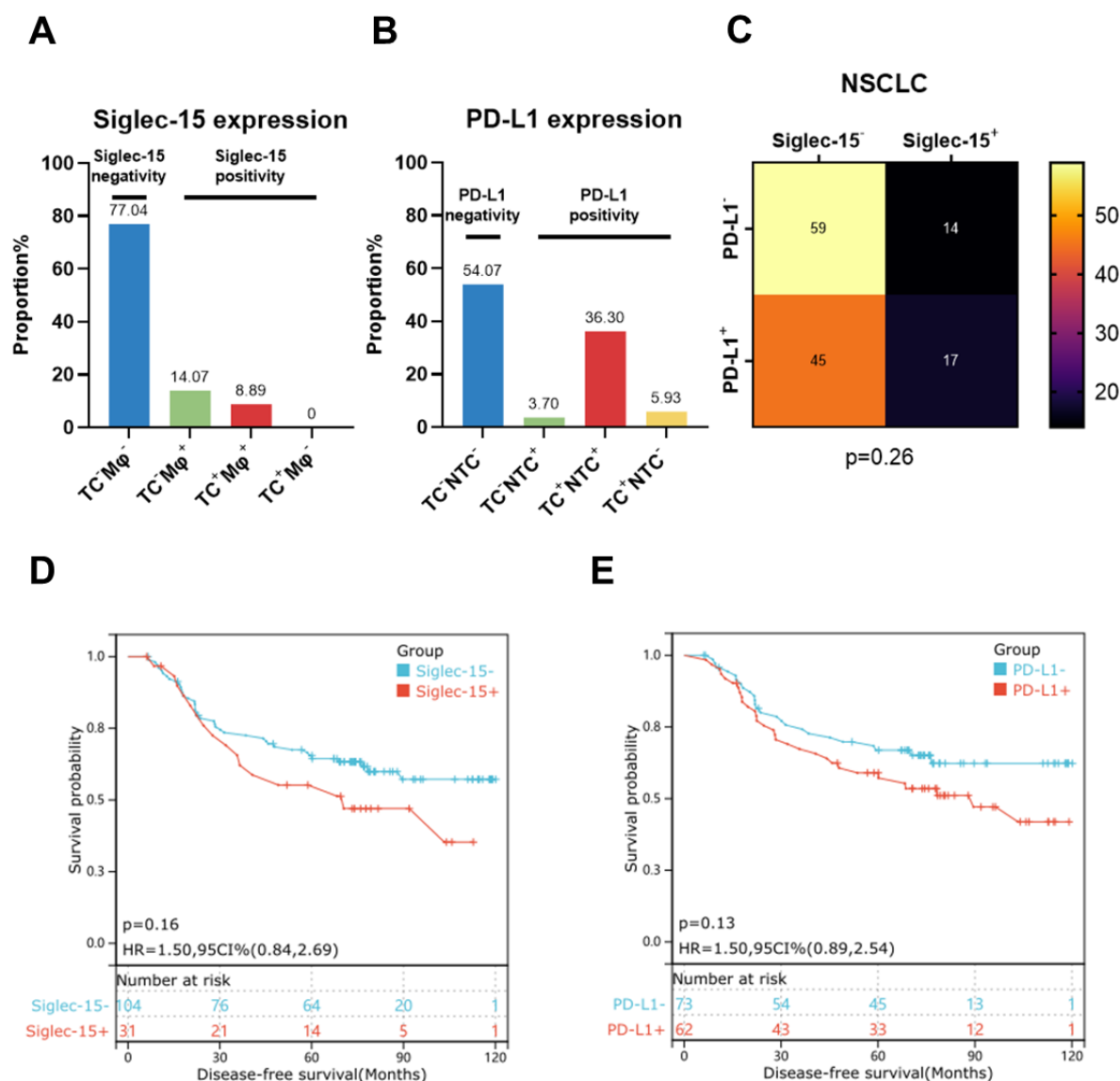


Fig. S3. Different expression patterns of Siglec-15 and PD-L1 in NSCLC. (A) NSCLC samples were divided into 4 groups according to their Siglec-15 expression patterns. (B) NSCLC samples were divided into 4 groups according to their PD-L1 expression patterns. (C) Chi-Square test showed the relationship between Siglec-15 and PD-L1. (D) Comparison of disease-free survival between patients with Siglec-15 positivity and negativity. (E) Comparison of disease-free survival between patients with PD-L1 positivity and negativity.

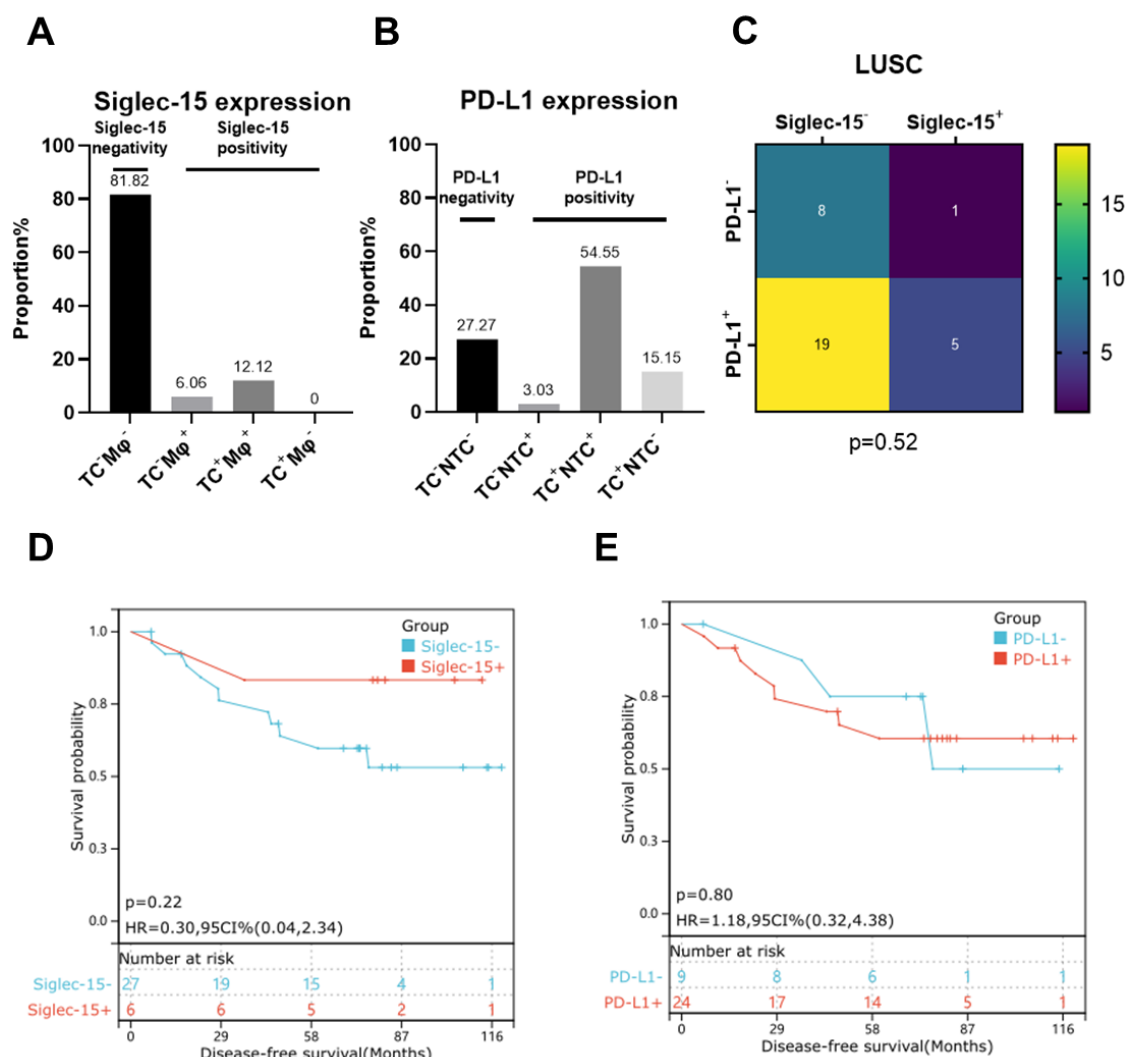


Fig. S4. Different expression patterns of Siglec-15 and PD-L1 in LUSC. (A) LUSC samples were divided into 4 groups according to their Siglec-15 expression patterns. (B) LUSC samples were divided into 4 groups according to their PD-L1 expression patterns. (C) Chi-Square test showed the relationship between Siglec-15 and PD-L1. (D) Comparison of disease-free survival between patients with Siglec-15 positivity and negativity. (E) Comparison of disease-free survival between patients with PD-L1 positivity and negativity.

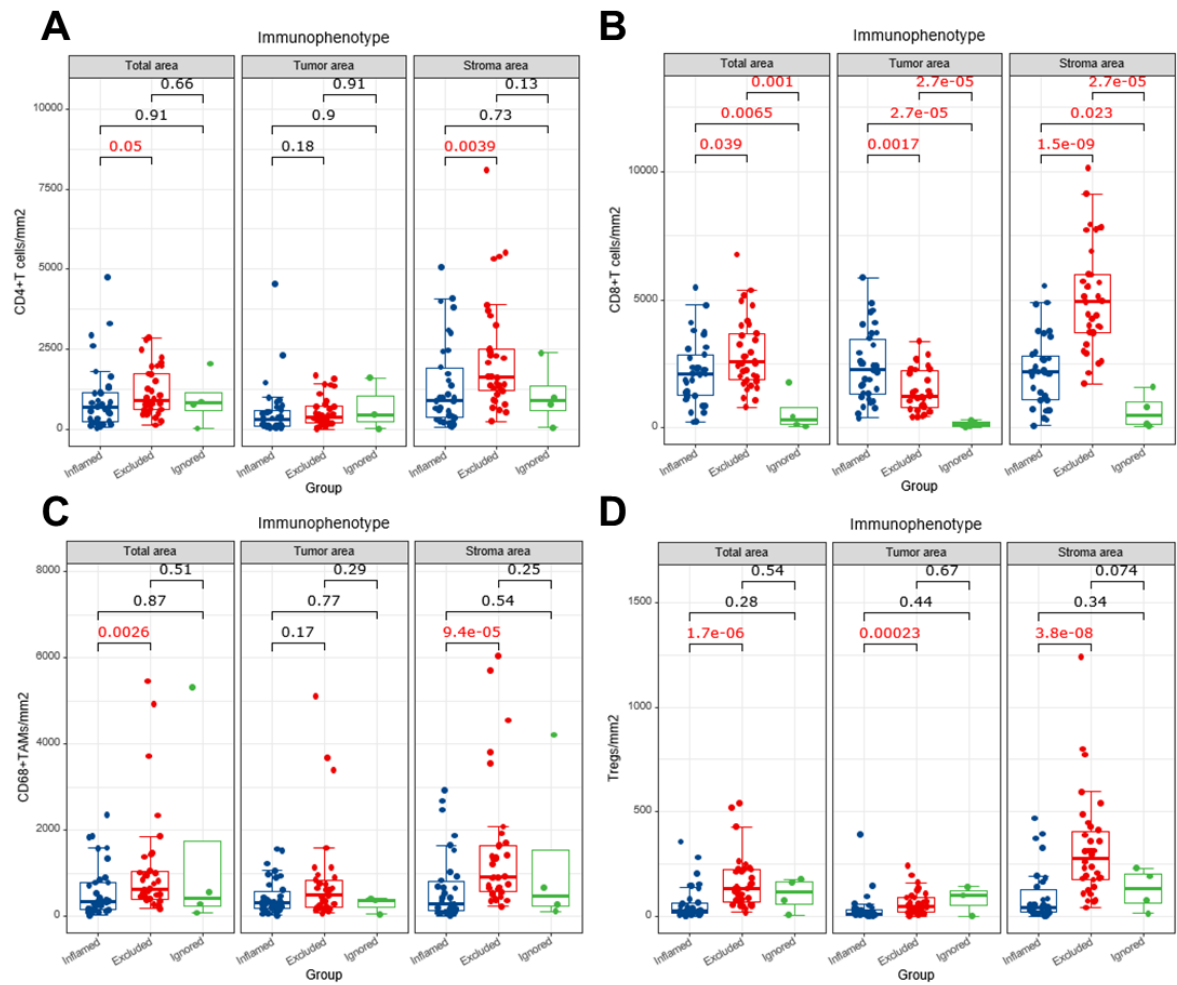


Fig. S5. Density of immune cells among the immunophenotypes. Among the immunophenotypes in non-metastasis LUAD patients, box plot showed the density of (A) CD4⁺T cells, (B) CD8⁺T cells, (C) CD68⁺TAMs and (D) CD4⁺FoxP3⁺Tregs. The bar indicates mean with 95% CI.

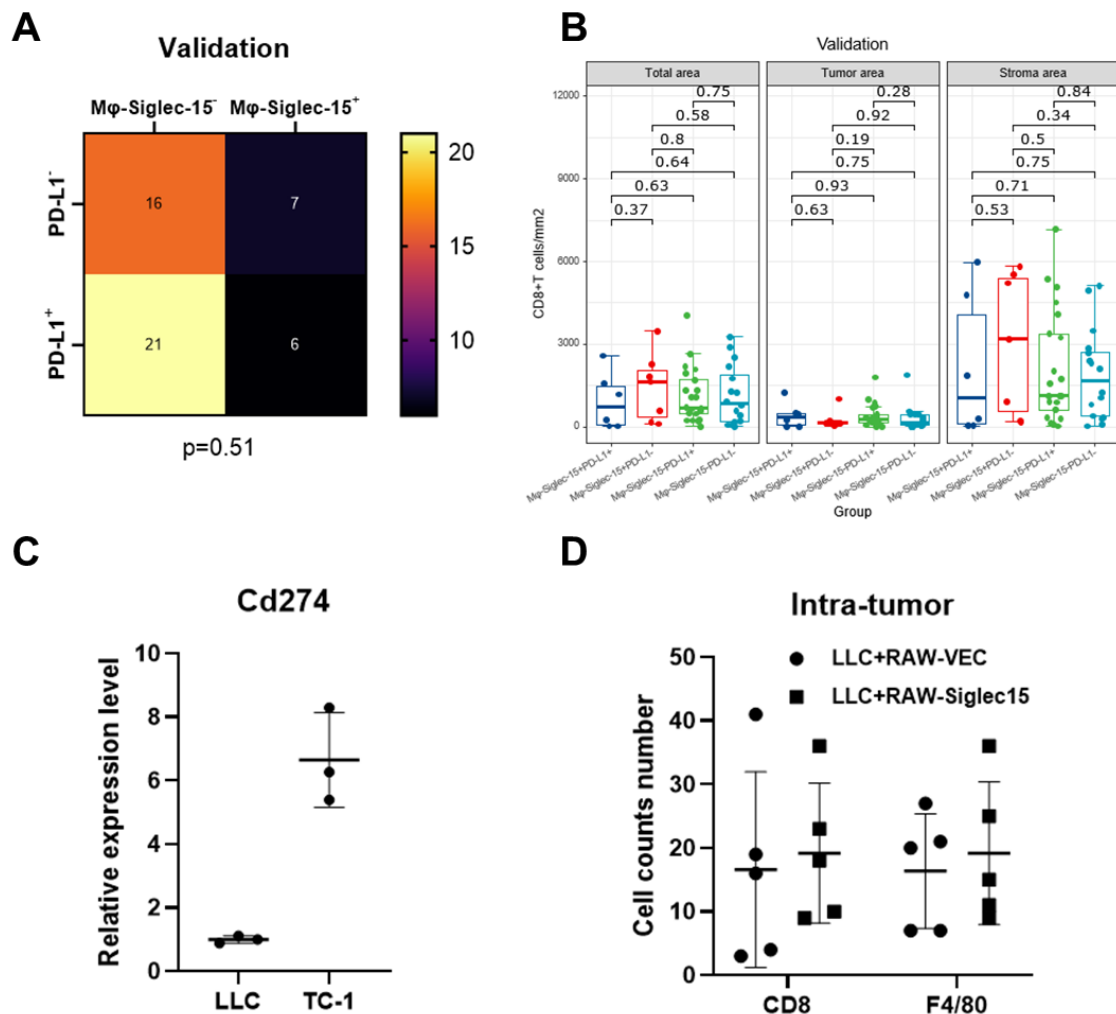


Fig. S6. Validation of the immunophenotypes.

(A) Chi-Square test showed the relationship between Mφ-Siglec-15 and PD-L1 in the validation cohort. (B) The density of CD8⁺T cells among Mφ-Siglec-15 and PD-L1 patterns in the validation cohort. The bar indicates mean with 95% CI. (C) The expression of Cd274 in LLC and TC-1 detected by qPCR (n = 3 per group). The bar indicates mean with SD. (D) Comparison of number of intra-tumor immune cells between two groups in vivo (n = 5 per group). The bar indicates mean with SD.