Table S1. Clinicopathological characteristics in each cohort.

Table S2. Immunohistochemistry (IHC) procedure and antibodies.

Table S3. Flow cytometry procedure and antibodies.

Table S4. Full multivariate Cox regression analysis for overall of patients with gastric cancer according to Lauren classification in Zhongshan TMA and TCGA cohort.

Figure S1. Differential expression of CD8⁺ T cell signature genes between intestinal and diffuse type gastric cancer patients in TCGA cohort.

Figure S2. Numbers and functional status of CD8⁺ T cells in peritumor gastric mucosa tissues.

Figure S3. Representative immunohistochemistry images of interleukin-10, transforming growth factor- β 1 and Indoleamine 2,3-Dioxygenase 1 in intestinal type and diffuse type gastric cancer.

Table S1. Clinicopathological characteristics in each cohort.

Group	Zhongshan TMA	TCGA cohort	Zhongshan FCM
	cohort		cohort
Number of patients	456	235	63
Gender			
Male	320	153	50
Female	136	82	13
Age (years)	60.0±11.7	64.3±10.6	66.5±8.4
Tumor size	3.8±2.2	-	4.4±2.4
Lauren classification			
Intestinal	281	159	36
Diffuse	169	76	27
pTNM stage			
Stage I	107	28	11
Stage II	107	60	18
Stage III	236	121	34
Stage IV	6	26	-
Tumor grade			
Grade 1	14	8	1
Grade 2	94	85	13
Grade 3	348	134	48
Grade X	-	8	1

Abbreviations: TNM = tumor node metastasis.

Table S2. Immunohistochemistry (IHC) procedure and antibodies.

No.	Antibody name	Description	Company	Catalog No.	Diluted
1	Anti-CD8 alpha antibody	Mouse	Abcam	Ab17147	1:100
		monoclonal			
2	Anti-Granzyme B	Rabbit	Abcam	Ab4059	1:100
		polyclonal			
2	Anti-IL-10 antibody	Mouse	Abcam	Ab134742	1:400
		monoclonal			
3	Anti- Indoleamine 2, 3-dioxygenase antibody	Mouse	Abcam	Ab55305	1:500
		monoclonal			
4	Anti-TGF-61 antibody	Goat monoclonal	R&D	Ab-246-NA	1:400

IHC procedures. Formalin-fixed paraffin-embedded surgical specimens were collected and used for tissue microarray construction and subsequent immunohistochemistry studies. Tissue blocks were sectioned at 4 mm diameter and mounted on glass slides. The slides were dewaxed in dry-heat oven, xylene and graded alcohols, and then washed with phosphate-buffered saline for 3 times. After treated with 3% H₂O₂ for 30 minutes at 37° C, the slides were boiled in sodium citrate buffer with a microwave oven for 14 minutes and then treated with 10% normal goat serum blocking solution for 120 minutes at 37° C. Primary antibodies (anti-CD8 alpha, Anti-Granzyme B, anti-IL-10, Anti-Indoleamine 2, 3-dioxygenase and anti-TGF- β 1; diluted as preceding described), were applied in a moist chamber at 4°C overnight. After washed off the primary antibody, the slides stained with secondary HRP-labeled antibody in blocking buffer for 1 hour at room temperature, then developed with DAB reagent for 2 minutes, and counterstained with hematoxylinan for 3 minutes.

Table S3. Flow cytometry procedure and antibodies.

No.	Antibody name	Description	Company	Catalog No.	Fluorochrome
1	Anti-CD45	Mouse monoclonal	Biolegend	368532	PE/Cy7
2	Anti-CD3	Mouse monoclonal	Biolegend	300328	PerCP/Cy5.5
3	Anti-CD8	Mouse monoclonal	BD	555366	FITC
4	Anti-Granzyme B	Mouse monoclonal	eBioscience	MA5-23688	PE
5	Anti-CD107a	Mouse monoclonal	BD	560664	APC
6	Anti-perforin	Mouse monoclonal	BD	563576	AF647
7	Anti-IFN gamma	Mouse monoclonal	eBioscience	56-7319-42	AF700
8	Anti-PD-1	Mouse monoclonal	BD	558694	APC
9	Anti-TIM-3	Mouse monoclonal	BD	563422	PE
10	Anti-CTLA-4	Mouse monoclonal	Biolegend	369610	BV605
11	Anti-LAG-3	Mouse monoclonal	Biolegend	369322	BV785

Flow cytometry protocol: For fresh tumor tissues, single cells were isolated by using collagenase IV. Approximately 1×10^{6} cells were centrifuged and incubated in RBC lysis buffer on ice for 15 minutes, incubated with Human TruStain FcX (Biolegend) for Fc receptor blocking and stained for surface markers in cell staining buffer for 30 minutes at 4°C in the dark. After being washed with cell staining buffer, cells were fixed with fixation buffer (Biolegend) and permeabilized with intracellular staining permeabilization wash buffer (Biolegend). Intracellular cytokine staining was then performed in intracellular staining permeabilization wash buffer for 30 minutes at 4°C in the dark. The primary antibody used for flow cytometry were as listed above.

Table S4. Full multivariate Cox regression analysis for overall survival of patients with gastric cancer according to Lauren classification in Zhongshan TMA and TCGA cohort.

Quit annua	Zhongshan TMA cohort		TCGA coho	TCGA cohort	
Subgroup	HR (95%CI)	P-value ^a	HR (95%CI)	P-value ^a	
All patients					
TNM stage: Stage 3+4 vs Stage 1+2	4.168 (3.001-5.772)	<0.001	2.347 (1.409-3.907)	0.001	
Tumor grade: Grade 3+X vs Grade 1+2	0.881(0.689-1.375)	0.881	1.200(0.959-1.500)	0.112	
Age: ≥65 vs < 65	1.093(0.831-1.437)	0.527	1.646 (1.058-2.562)	0.028	
Sex: female vs male	1.308(0.985-1.736)	0.065	0.873(0.549-1.388)	0.567	
CD8+ T cells: high vs low	0.788(0.604-1.028)	0.080	0.615(0.390-0.968)	0.037	
Intestinal type					
TNM stage: Stage 3+4 vs Stage 1+2	4.060 (2.670-6.175)	<0.001	2.436(1.282-4.629)	0.007	
Tumor grade: Grade 3+X vs Grade 1+2	0.757 (0.509-1.127)	0.173	1.256(0.963-1.638)	0.095	
Age: ≥65 vs < 65	1.227(0.860-1.750)	0.261	1.744(0.994-3.058)	0.054	
Sex: female vs male	1.508(1.032-2.204)	0.035	1.213(0.699-2.103)	0.495	
CD8 ⁺ T cells: high vs low	0.514(0.358-0.736)	<0.001	0.543(0.323-0.913)	0.022	
Diffuse type					
TNM stage: Stage 3+4 vs Stage 1+2	4.572 (2.694-7.759)	<0.001	2.591(1.076-6.237)	0.035	
Tumor grade: Grade 3+X vs Grade 1+2	1.722 (0.544-5.455)	0.358	0.863(0.411-1.815)	0.699	
Age: ≥65 vs < 65	1.018(0.657-1.578)	0.937	1.061(0466-2.416)	0.888	
Sex: female vs male	1.091(0.711-1.671)	0.692	0.387(0.149-1.004)	0.052	
CD8 ⁺ T cells: high vs low	1.306(0.834-2.046)	0.247	1.169(0.395-3.455)	0.779	
Abbreviations: HR = Hazard Ratio; 95%CI= 95% confidence interval.					

^a*P*-value<0.05 marked in bold font shows statistically significant.



Figure S1. Differential expression of CD8⁺ T cell signature genes between intestinal and diffuse type gastric cancer patients in TCGA cohort. (A). A 2D heatmap showing different expression of CD8⁺T cell signature genes between intestinal (n=169) and diffuse type (n=76) gastric cancer patients in TCGA cohort. (B). Average expression of CD8⁺ T cell signature genes in intestinal type (n=169) and diffuse type (n=76) gastric cancer patients from the TCGA cohort. TCGA = The Cancer Genome Atlas.



Figure S2. Numbers and functional status of CD8⁺ T cells in peritumor gastric mucosa tissues. (A). Peritumoral CD8⁺ T cell infiltration density in intestinal type (n=286) and diffuse type (n=170) gastric cancer patients from Zhongshan TMA cohort. (B). Proportions among all CD45⁺ leukocytes and absolutes numbers of CD8⁺ T cells in intestinal type (n=9) and diffuse type (n=7) gastric cancer patients detected by flow cytometry. (C). Flow cytometrical analysis of effector molecules CD107a, GZMB, PRF1 and IFN-γ expression in CD8⁺ T cells from

peritumor tissues with intestinal (n=9) and diffuse (n=7) type gastric cancer. (D). Flow cytometrical analysis of effector molecules PD-1, CTLA-4, TIM-3 and LAG-3 expression in CD8⁺ T cells from peritumor tissues with intestinal (n=9) and diffuse (n=7) type gastric cancer. GZMB = granzyme B; IFN- γ = interferon gamma; PRF1=perforin; PD-1 = programmed cell death 1; CTLA-4 = cytotoxic T lymphocyte associated protein-4; TIM-3= T cell immunoglobulin domain and mucin domain-3; LAG-3 = lymphocyte activation gene-3; n. s = no significance.



