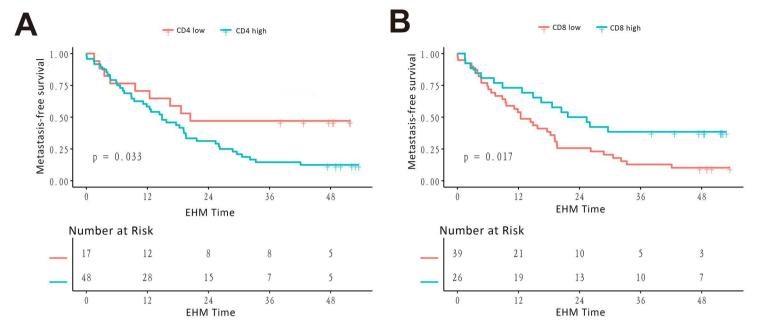


Fig. S1. (A) Calculating the best cut-off value of CD4+ using a spline smoothing plot. (B) Calculating the best cut-off value of CD8+ using a spline smoothing plot. (C)Calculating the best cut-off value of Treg cells using a spline smoothing plot.



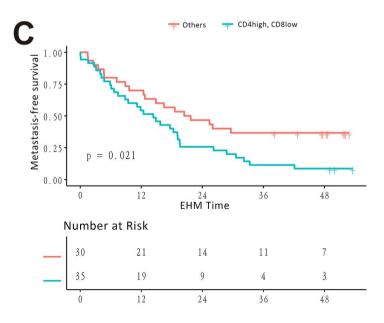


Fig. S2 Kaplan-Meier analyses for MFS according to CD4+ cell ratio (A), CD8+ cell ratio (B), and combined (CD4+/CD8+) cell ratio (C) in the validation cohort.

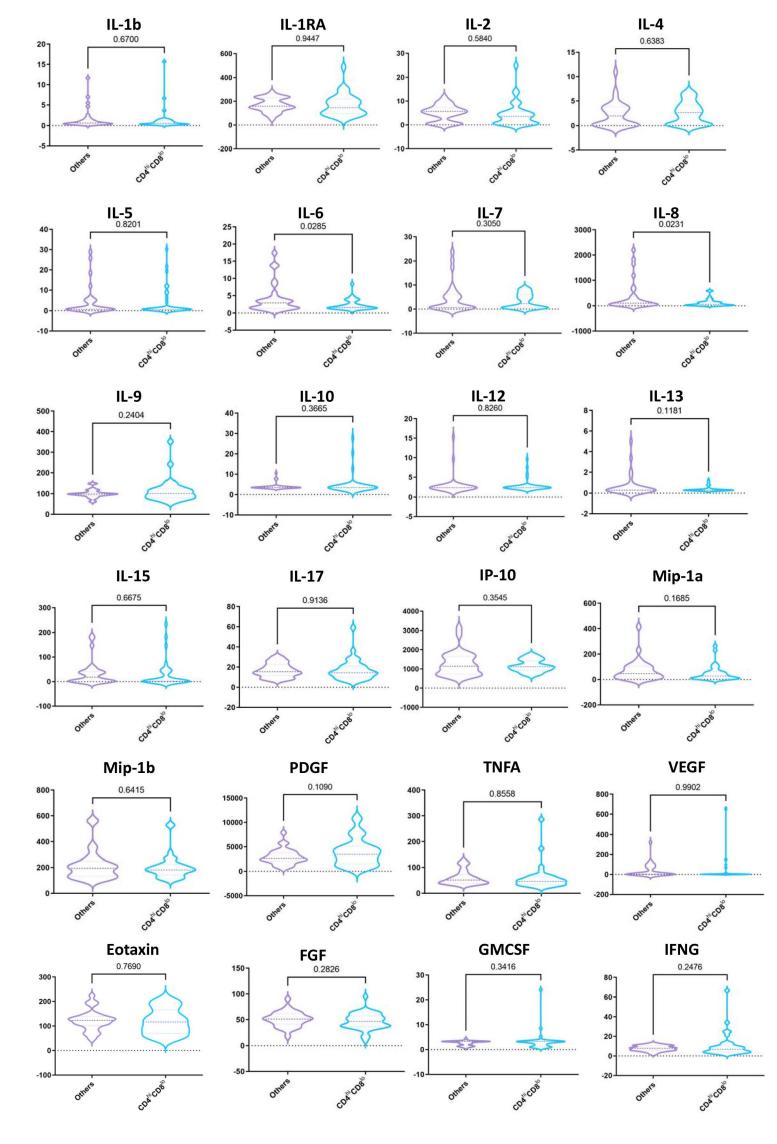


Fig. S3. Difference in 24 serum cytokine levels between HCC patients with the CD4high/CD8low phenotype and other pooled patients.

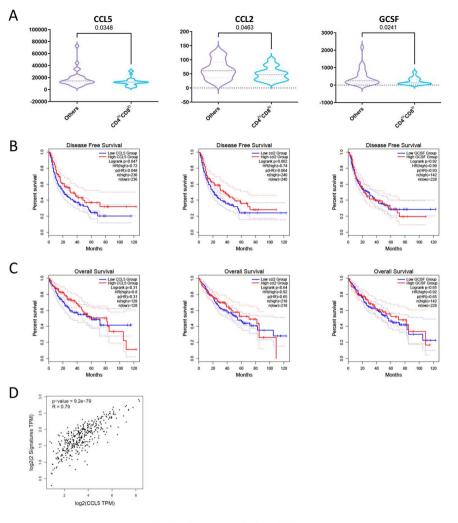


Fig. S4 CCL5 affects DFS for HCC patients.

(A) Differences in CCL5, CCL2, and GCSF levels in HCC patients with different systemic immune states.

(B, C) The prognosis value of CCL5, CCL2, and GCSF expression levels.

Patients were divided into 2 groups according to the values of CCL5, CCL2, and GCSF expression.

Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan-Meier method.

(D) Correlation analysis between CCL5 (R = 0.79), CCL2 (R = 0.52),

and T-lymphocyte gene signatures (CD4/CD8) using the Spearman method.

Characteristic	Non-EHM (N=135)	EHM (N=180)	<i>p</i> -value
AGE	58.6 ± 10.5	58.9 ± 10.4	0.678
SEX			0.068
Male	98 (72.6%)	151 (83.9%)	
Female	37 (27.4%)	29 (16.1%)	
Hepatitis			0.901
None	15 (11.1%)	19 (10.6%)	
HBV	100 (74.1%)	135 (75.0%)	
HCV	17 (12.6%)	19 (10.6%)	
HBV&HCV	1 (0.7%)	3 (1.7%)	
Others	2 (1.5%)	4 (2.2%)	
Tumor Number	1.4 ± 0.8	1.9 ± 1.6	0.002*
Tumor size	2.7 ± 1.2	2.8 ± 1.5	0.727
AFP	173.5 ± 622.1	312.3 ± 2047.9	0.264
HB	135.9 ± 17.5	133.2 ± 19.7	0.260
PLTs	132.6 ± 59.4	126.0 ± 59.4	0.385
Prothrombin	14.4 ± 3.4	14.2 ± 1.1	0.619
Albumin	40.7 ± 4.5	39.7 ± 4.3	0.073
WBC	4.8 ± 1.7	4.6 ± 1.6	0.347
Lymphocytes	0.3 ± 0.1	0.3 ± 0.1	0.211
Neutrophiles	0.6 ± 0.1	0.6 ± 0.1	0.232
BCLC.Staging			0.015*
А	121 (89.6%)	143 (79.4%)	
В	14 (10.4%)	37 (20.6%)	
Child-Pugh Grade			0.321
А	135 (100.0%)	177 (98.3%)	
В	0 (0.0%)	1 (0.6%)	
С	0 (0.0%)	2 (1.1%)	

Table S1. Patient characteristics in non- and EHM population of primary cohort.

The bold value indicated identifying significant patient characteristics with baseline differences between two groups. *:P < 0.05.

Characteristic	Non-EHM (N=14)	EHM (N=51)	<i>p</i> -value
AGE	55.9 ± 7.1	60.5 ± 10.1	0.063
SEX			0.365
Male	10 (71.4%)	42 (82.4%)	
Female	4 (28.6%)	9 (17.6%)	
Hepatitis			0.539
None	3 (21.4%)	10 (19.6%)	
HBV	11 (78.6%)	34 (66.7%)	
HCV	0 (0.0%)	4 (7.8%)	
HBV&HCV	0 (0.0%)	3 (5.9%)	
Others	2 (1.7%)	3 (2.0%)	
Tumor.Number	1.2 ± 0.4	2.1 ± 1.6	0.072
Tumor size	2.4 ± 1.0	2.8 ± 1.3	0.291
AFP	391.3 ± 632.5	1159.0 ± 3938.2	0.474
HBs	137.0 ± 13.9	134.2 ± 17.4	0.602
PLTs	128.4 ± 52.5	126.6 ± 52.0	0.918
Prothrombin	14.3 ± 0.7	14.2 ± 1.0	0.741
Albumin	40.8 ± 4.1	39.3 ± 4.8	0.313
WBC	5.2 ± 2.3	4.9 ± 1.7	0.688
Lymphocytes	0.3 ± 0.1	0.3 ± 0.1	0.171
Neutrophiles	0.6 ± 0.1	0.6 ± 0.1	0.354
BCLC.Staging			0.035*
А	14 (100.0%)	38 (74.5%)	
В	0 (0.0%)	13 (25.5%)	
Child-Pugh Grade			0.320
А	13 (92.9%)	50 (98.0%)	
В	1 (7.1%)	1 (2.0%)	

Table S2. Patient characteristics in non- and EHM population of validation cohort.

The bold value indicated identifying significant patient characteristics with baseline differences between two groups. *:P < 0.05.

	(Groups	1-years MFS	3-years MFS	5-years MFS	7-years MFS	10-years MFS	HR, 95%CI	р	Median (months)
CD4 ⁺ cratio	cell	CD4 ^{high} (>25)	69%	51%	39%	31%	21%	1.7(1.2-2.3)	<i>p</i> =0.0019	38.4
		$CD4^{low} (\leq 25)$	80%	67%	57%	50%	39%			85.7
CD8 ⁺ c ratio	cell	CD8 ^{high} (>30)	78%	64%	54%	47%	35%	0.6(0.4-0.8)	<i>p</i> <0.001	77.7
		CD8 ^{low} (≤25)	65%	46%	34%	27%	16%			28.8
Combined	ad	$CD4^{high}/CD8^{low}$	63%	42%	30%	21%	12%	2.0(1.5-2.8) <i>p</i> <0.001	26	
	Ju	Remaining patients	80%	65%	55%	46%	35%		<i>p</i> <0.001	77.7

Table S3. Tumor extrahepatic metastasis rate at 1-yr, 3-yr, 5-yr, 7-yr and 10-yr after thermal ablation