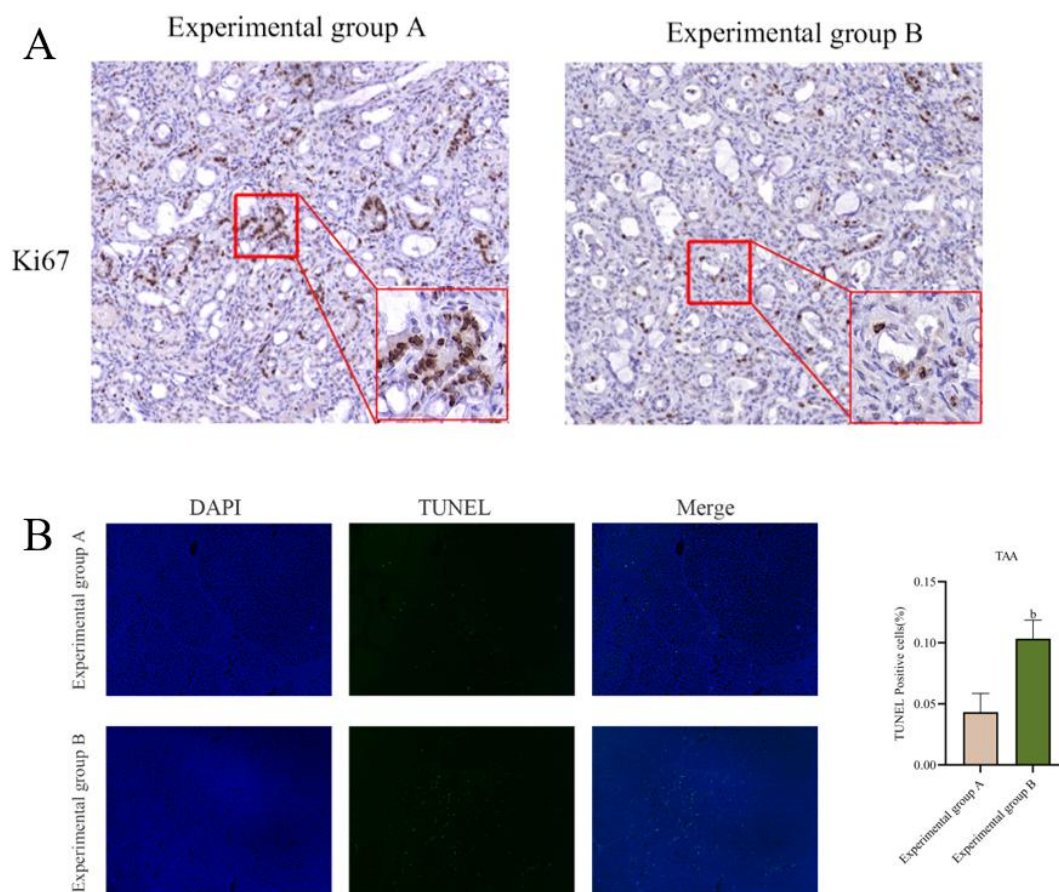


Supplementary Figure 1 Determination of RcIL-22 concentration. As shown in the figure, when the concentration of RcIL-22 was 50 mg/kg, compared with the control group, the expression level of p-ERK1/2 was the highest ($^dP < 0.0001$). When the concentration continued to increase, the expression level of p-ERK1/2 was not significantly different from before.



Supplementary Figure 2 The results of Ki67 immunohistochemical staining and immunofluorescence TUNEL assays, as well as the quantitative analysis results, for liver tumor tissue sections from experimental group A and experimental group B. A: Representative immunohistochemical staining of Ki67 in tumor tissues from experimental groups A and B (scale bar, 100 μ m); B: Fluorescent TUNEL assay results and quantitative analysis in tumor tissues from experimental groups A and B. The TUNEL results of experimental group A showed a statistically significant difference compared to the TUNEL results of the experimental group B. ^b $P < 0.01$.

Supplementary Table 1 Detailed clinical information for all patients ($n = 27$), n (%)

Characteristics	Number of patients
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Gender	
Male	16 (59.3)
Female	11 (40.7)
Age	
<60	9 (33.3)
≥60	18 (66.7)
TNM stage	
I	1 (3.7)
II	9 (33.3)
III	17 (63)
IV	0
Regional lymph nodes	
N0	7 (25.9)
N1	20 (74.1)
Distant metastasis	
No	22 (81.5)
Yes	5 (18.5)
Tumor occurrence site	
iCCA	14 (51.9)
pCCA	9 (33.3)
dCCA	4 (14.8)

Supplementary Table 2 Reagents information

Antibody name	Cat No	Brand	Application	Dilution rate
IL-22	WL04441	Wanleibio, Shenyang, China	WB	1:1500
IL-22R1	DF13375	Affinity, Jiangsu, China	WB	1:1000
KI67	AF0198	Affinity, Jiangsu,	IHC	1:100

		China		
STAT3	AF6294	Affinity, Jiangsu,	WB	1:1000
		China		
P-STAT3	AF3293	Affinity Jiangsu,	WB	1:1000
		China		
ERK	AF0155	Affinity, Jiangsu,	WB	1:2000
		China		
P-ERK	AF1015	Affinity Jiangsu,	WB	1:1000
		China		
Bcl2	AF6139	Affinity, Jiangsu,	WB	1:1000
		China		
BAX	AF0120	Affinity, Jiangsu,	WB	1:2000
		China		
MMP7	AF0218	Affinity, Jiangsu,	WB	1:2000
		China		
MMP9	AF5228	Affinity, Jiangsu,	WB	1:1000
		China		
N-cadherin	22018-1-AP	Proteintech,	WB	1:6000
		Wuhan, China		
E-cadherin	60335-1-Ig	Proteintech,	WB	1:6000
		Wuhan, China		
Vimentin	AF7013	Affinity, Jiangsu,	WB	1:1000
		China		
Cytokeratin 19	AF0192	Affinity, Jiangsu,	IHC	1:100
		China		
Interleukin-22	GP20620	Glpbio,		
Human		California,		
Recombinant		United States		
Interleukin-22	GP20623	Glpbio,		

Rat	California,
Recombinant	United States

WB: Western blot; IHC: Immunohistochemistry.

Supplementary Table 3 Primer sequences for PCR amplification

Gene	Forward primer	Reverse primer
<i>IL-22R1</i>	ATCTGCTCCAGCACGTGAAA	CAGGTGGCTTGAGGGTAGTG

Supplementary Table 4 The biochemical indices of liver function in different groups of rats(mean±SD)

	NC (<i>n</i> = 3)	Experimental group A (<i>n</i> = 3)	Experimental group B (<i>n</i> = 3)
ALT(U/L)	35.80 ± 7.21	113.30 ± 2.33	101.80 ± 2.05
AST(U/L)	80.27 ± 1.99	221.20 ± 2.04	163.70 ± 1.31
ALP(U/L)	177.10 ± 9.16	379.40 ± 4.20	208.80 ± 7.90
T-Bil(μmol /L)	1.22 ± 0.05	3.42 ± 0.28	2.47 ± 0.04

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; T-Bil: Total bilirubin.