Supplementary Table 1 Baseline characteristics of LARC patients in the FMUUH cohort

Variables	**(n=118)**
Sex (%)	
Male	75 (63.6)
Female	43 (36.4)
Age (years)	54.3 ± 13.3
Distance from the anal verge (cm)	5.6 ± 1.7
Tumor differentiation (%)	
Well or moderately differentiated	85 (72.0)
Poorly differentiated and others [a]	33 (28.0)
Histopathology (%)	
Adenocarcinoma	93 (78.8)
Mucinous or signet ring adenocarcinoma	25 (21.2)
TRG (%)	
0	21 (17.8)
1	25 (21.2)
2	48 (40.7)
3	24 (20.3)
ypTNM stage (%)	
0	23 (19.5)
I	23 (19.5)
II	34 (28.8)
III	38 (32.2)

Data are expressed as number (%) or as median ± standard deviation, where appropriate.

SD: standard deviation; CEA: carcinoembryonic antigen; TRG: tumor regression grade; ypTNM stage: post-chemoradiotherapy pathological TNM stage

[a] including mucinous and signet cell carcinoma

Supplementary Table 2 Ten hub genes in the coexpression Tan module

Official symbol	Official full name	Also known as	Gene ID	Location
NOTCH3	notch receptor 3	CADASIL, CADASIL1, CASIL, IMF2, LMNS	4854	19p13.12
SPARC	secreted protein acidic and cysteine rich	BM-40, OI17, ON, ONT	6678	5q33.1
DCN	decorin	CSCD, DSPG2, PG40, PGII, PGS2, SLRR1B	1634	12q21.33
ITGB1	integrin subunit beta 1	CD29, FNRB, GPIIA, MDF2, MSK12, VLA-BETA, VLAB	3688	10p11.22
MMP2	matrix metallopeptidase 2	CLG4; MONA; CLG4A; MMP-2; TBE-1; MMP-II	4313	16q12.2
THBS2	thrombospondin 2	TSP2	7058	6q27
COL15A1	collagen type XV alpha 1 chain	/	1306	9q22.33
CD34	CD34 molecule	/	947	1q32.2
PDGFRB	platelet derived growth factor receptor beta	IMF1; KOGS; IBGC4; JTK12; PDGFR; PENTT; CD140B; PDGFR1; PDGFR-1	5159	5q32
SERPINH1	serpin family H member 1	CBP1; CBP2; OI10; gp46; AsTP3; HSP47; PIG14; PPROM; RA-A47; SERPINH2	871	11q13.5

Supplementary Table 3 Cox regression analysis of predictors for disease-free survival in patients with rectal cancer patients in the FMUUH cohort (n=118)

Genes	Univariate			Multivariate		
	HR	**95% CI**	***P* value**	**HR**	**95% CI**	***P* value**
NOTCH3	2.370	1.679-3.344	<0.001	1.668	1.087-2.559	0.019
SPARC	2.762	1.880-4.057	<0.001	1.849	1.241-2.756	0.003
DCN	0.468	0.333-0.657	<0.001	0.607	0.385-0.959	0.032
ITGB1	4.129	2.614-6.521	<0.001	1.773	1.006-3.126	0.048
MMP2	1.958	1.393-2.752	<0.001	1.265	0.845-1.893	0.253
THBS2	0.437	0.302-0.631	<0.001	0.790	0.553-1.130	0.198
COL15A1	0.693	0.520-0.924	0.012	0.752	0.473-1.195	0.227
CD34	0.533	0.386-0.737	<0.001	0.650	0.396-1.068	0.089
PDGFRB	1.020	0.774-1.344	0.887			
SERPINH1	1.044	0.742-1.468	0.805			

FMUUH: Fujian Medical University Union Hospital; HR: hazard ratio; CI: confidence interval

Supplementary Table 4 Association between risk score and clinicopathological characteristic of LARC patients in the FMUUH cohort (n=118)

Characteristics	Risk score		*P* value
	Low (n=59)	High (n=59)	
Gender (%)			0. 566
Male	36 (61.0)	39 (66.1)	
Female	23 (39.0)	20 (33.9)	
Age (years)	54.7 ± 12.5	53.9 ±14.1	0.731
BMI (kg/m^2)	22.6 ± 2.9	22.6 ± 3.4	0. 979
Distance from the anal verge (cm)	5.6 ± 1.6	5.5 ±1.7	0. 651
Histopathology (%)			0.499
Adenocarcinoma	48 (81.4)	45 (76.3)	
Mucinous or signet ring adenocarcinoma	11 (18.6)	14 (23.7)	
Tumor differentiation (%)			0.151
Well/moderately differentiated	46 (78.0)	39 (66.1)	
Poorly differentiated	13 (22.0)	20 (33.9)	
TRG (%)			<0.001
0	19 (32.2)	2 (3.4)	
1	12 (20.3)	13 (22.0)	
2	21 (35.6)	27 (45.8)	
3	7 (11.9)	17 (28.8%)	
ypTNM stage (%)			<0.001
0	21 (35.6)	2 (3.4)	
I	15 (25.4)	8 (13.6)	
II	14 (23.7)	20 (33.9)	
III	9 (15.3)	29 (49.2)	

Data are expressed as number (%) or as median ± standard deviation, where appropriate.

LARC: locally advanced rectal cancer; FMUUH: Fujian Medical University Union Hospital; BMI: body mass index; TRG: tumor regression grade; ypTNM stage: post-chemoradiotherapy pathological TNM stage

Supplementary Table 5 Cox regression analysis of predictors for DFS in patients with LARC following NCRT in the FMUUH cohort (n=118)

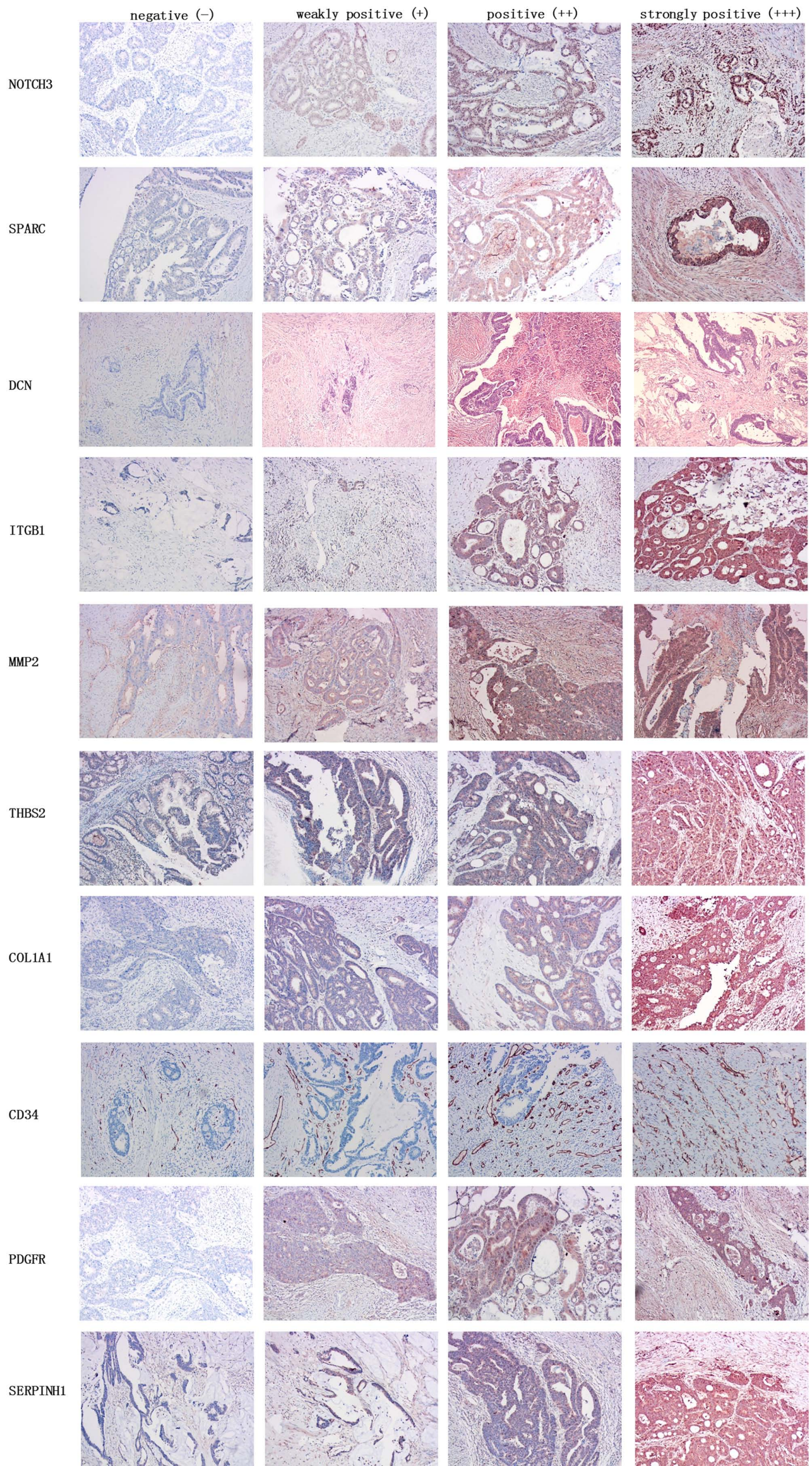
Factors	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Sex, male/female	1.076	0.555-2.087	0.827			
Age	0.996	0.972-1.020	0.716			
ASA score	0.963	0.526-1.763	0.902			
BMI	0.978	0.883-1.083	0.667			
Tumor distance from the anal verge	1.043	0.879-1.237	0.630			
Tumor size	1.225	0.905-1.659	0.189			
Preoperative chemotherapy regimen (oxaliplatin based vs. fluoropyrimidine only)	0.533	0.164-1.731	0.295			
Time interval to surgery	1.007	0.912-1.112	0.889			
Surgery approach (laparoscopic vs. open)	0.889	0.475-1.665	0.713			
Histopathology (mucinous or signet ring adenocarcinoma vs. adenocarcinoma)	0.776	0.343-1.754	0.542			
Tumor differentiation (poorly differentiated vs. well/moderately differentiated)	1.369	0.706-2.654	0.352			
Preoperative CEA level	0.996	0.975-1.018	0.713			
TRG	1.587	1.123-2.244	0.009	0.515	0.311-0.853	0.010
ypTNM stage	2.323	1.582-3.409	<0.001	1.682	1.035-2.73	0.036
IMA nodal metastasis	5.504	1.679-18.044	0.005	1.568	0.458-5.366	0.474
CRM involvement	4.751	1.118-20.182	0.035	1.332	0.294-6.032	0.709
Risk score	2.661	1.999-3.542	<0.001	2.855	2.038-4.000	<0.001

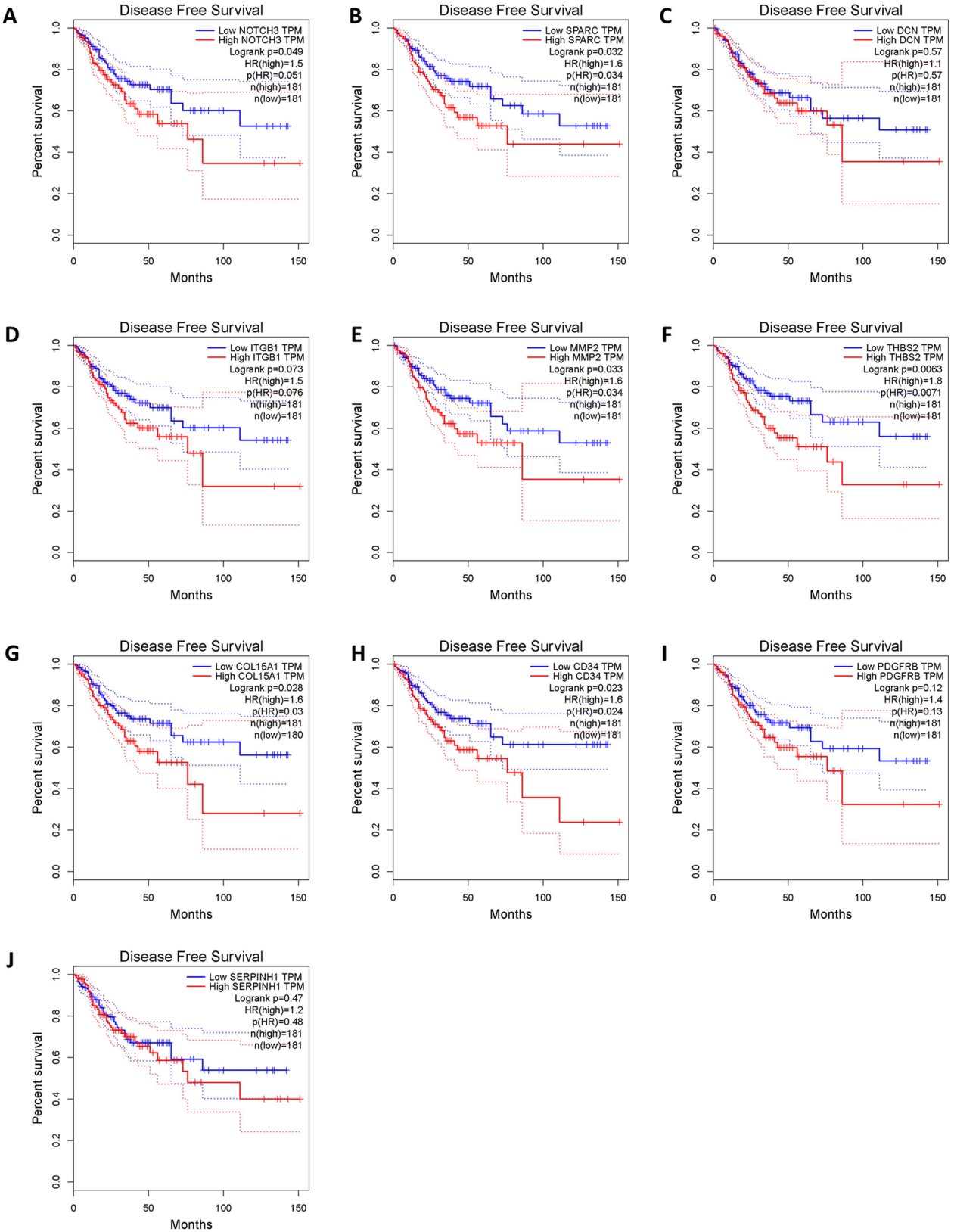
DFS: disease-free survival; LARC: locally advanced rectal cancer; NCRT: neoadjuvant chemoradiotherapy; MUUH: Fujian Medical University Union Hospital; HR: hazard ratio; CI: confidence interval; ASA: American Society of Anesthesiologists; BMI: body mass index; CEA: carcinoembryonic antigen; TRG: tumor regression grade; ypTNM stage: post-chemoradiotherapy pathological TNM stage; IMA: inferior mesenteric artery; CRM: circumferential resection margin.

Supplementary Figure legend

Figure s1 Immunostaining expression of the ten hub genes

Figure s2 Validation of the expression of the ten hub genes in TCGA using GEPIA


negative (−)
weakly positive (+)
positive (++)
strongly positive (+++)
NOTCH3
SPARC
DCN
ITGB1
MMP2
THBS2
COL1A1
CD34
PDGFR
SERPINH1


A
Disease Free Survival
Low NOTCH3 TPM
High NOTCH3 TPM
Logrank p=0.049
HR(high)=1.5
p(HR)=0.051
n(high)=181
n(low)=181
Percent survival
Months
B
Disease Free Survival
Low SPARC TPM
High SPARC TPM
Logrank p=0.032
HR(high)=1.6
p(HR)=0.034
n(high)=181
n(low)=181
Percent survival
Months
C
Disease Free Survival
Low DCN TPM
High DCN TPM
Logrank p=0.57
HR(high)=1.1
p(HR)=0.57
n(high)=181
n(low)=181
Percent survival
Months
D
Disease Free Survival
Low ITGB1 TPM
High ITGB1 TPM
Logrank p=0.073
HR(high)=1.5
p(HR)=0.076
n(high)=181
n(low)=181
Percent survival
Months
E
Disease Free Survival
Low MMP2 TPM
High MMP2 TPM
Logrank p=0.033
HR(high)=1.6
p(HR)=0.034
n(high)=181
n(low)=181
Percent survival
Months
F
Disease Free Survival
Low THBS2 TPM
High THBS2 TPM
Logrank p=0.0063
HR(high)=1.8
p(HR)=0.0071
n(high)=181
n(low)=181
Percent survival
Months
G
Disease Free Survival
Low COL15A1 TPM
High COL15A1 TPM
Logrank p=0.028
HR(high)=1.6
p(HR)=0.03
n(high)=181
n(low)=180
Percent survival
Months
H
Disease Free Survival
Low CD34 TPM
High CD34 TPM
Logrank p=0.023
HR(high)=1.6
p(HR)=0.024
n(high)=181
n(low)=181
Percent survival
Months
I
Disease Free Survival
Low PDGFRB TPM
High PDGFRB TPM
Logrank p=0.12
HR(high)=1.4
p(HR)=0.13
n(high)=181
n(low)=181
Percent survival
Months
J
Disease Free Survival
Low SERPINH1 TPM
High SERPINH1 TPM
Logrank p=0.47
HR(high)=1.2
p(HR)=0.48
n(high)=181
n(low)=181
Percent survival
Months