

Figure S1-5 and Table S1-3

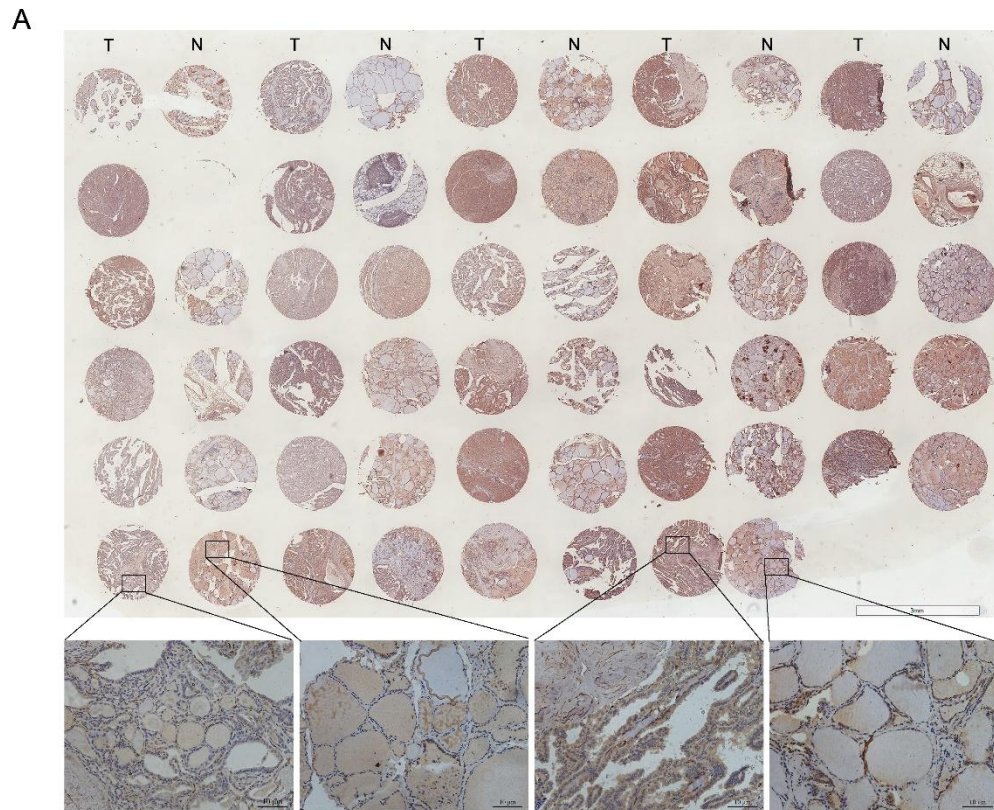


Figure S1 IHC staining of CDH4 in 29 paired papillary thyroid cancer tissues and adjacent normal tissues. **A** IHC staining of CDH4 in a tissue microarray containing 29 paired papillary thyroid cancer tissues and adjacent normal tissues.

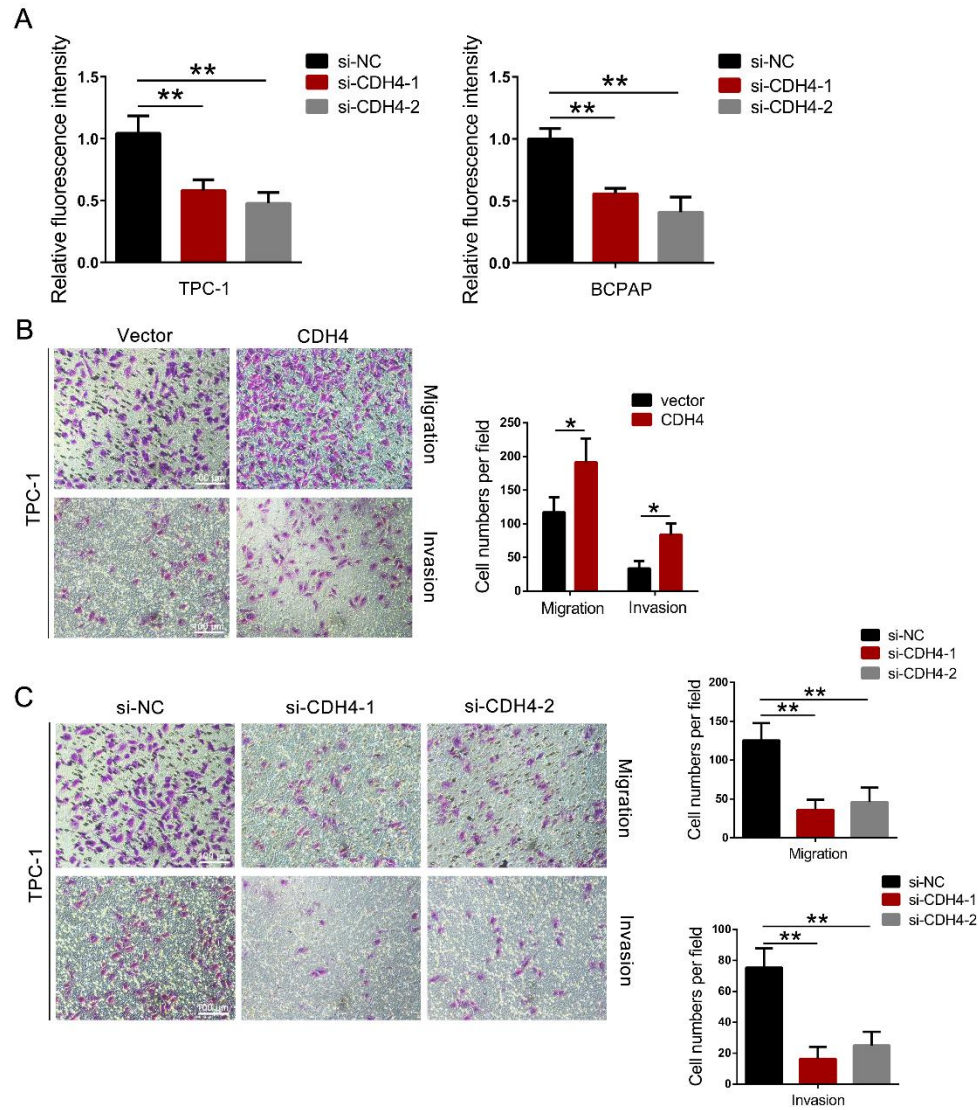


Figure S2 CDH4 promoted the cell migration and invasion of TPC-1 cell line. **A** Quantification of the immunofluorescence intensity of CDH4 in TPC-1 and BCPAP cells transfected with CDH4-tagerting siRNA or control siRNA. **B-C** Representative images and histogram analysis of TPC-1 cell migration and invasion following overexpression of CDH4 (**B**) or knockdown of CDH4 (**C**). *, $P < 0.05$; **, $P < 0.01$.

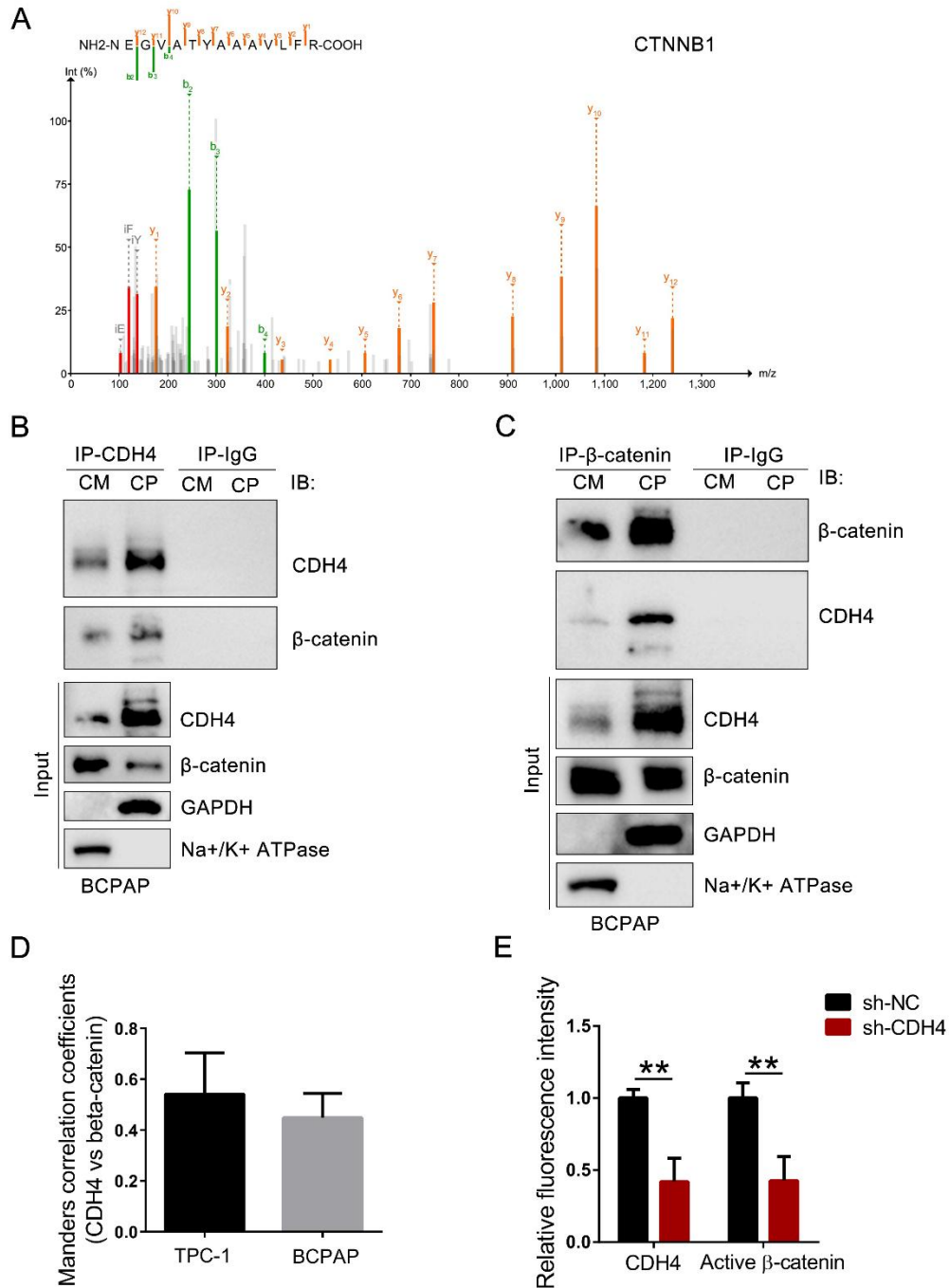


Figure S3 Cytosolic CDH4 interacted with β-catenin in BCPAP cells. **A** Mass spectrometry image of β-catenin. **B-C** Immunoprecipitation of CDH4 (**B**) or β-catenin (**C**) after cytosol-membrane fractionation in BCPAP cells. **D** Quantification of colocalization between CDH4 and β-catenin in PTC cells. **E** Quantification of the immunofluorescence intensity of CDH4 and active β-catenin in TPC-1 transfected with CDH4-tagerting shRNA or control

shRNA. **, $P < 0.01$.

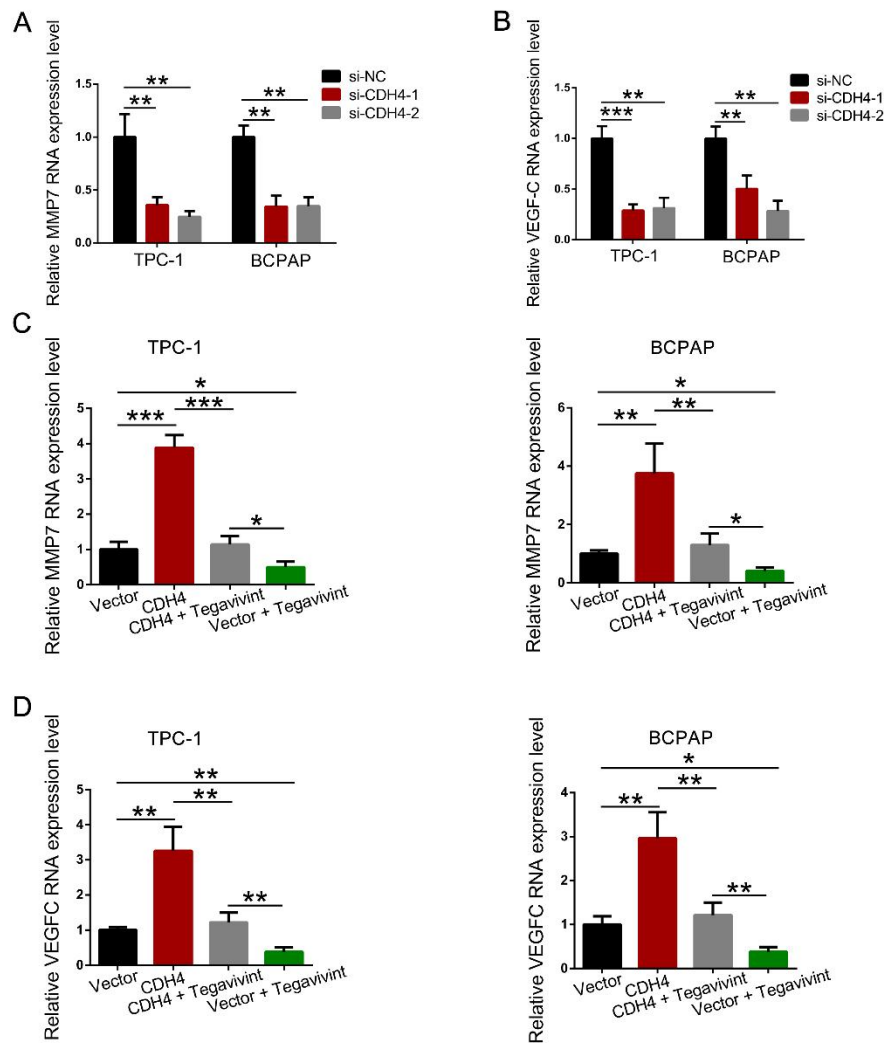


Figure S4 CDH4 regulated β -catenin-dependent transcriptional activation of MMP7 and VEGF-C. **A-B** The RNA level of MMP7 (**A**) and VEGF-C (**B**) was detected in PTC cells transiently transfected with CDH4-targeting siRNA or control siRNA. **C-D** PTC cells overexpressing CDH4 were treated with Tegavivint (100 nmol/L, 24h) as indicated, and qRT-PCR analysis of the RNA level of MMP7 (**C**) and VEGF-C (**D**) was conducted. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Table S1 siRNA and shRNA used in this study.

	5' to 3'
si-CDH4-1	CCACGUUUUCAGCUGUGGATT
si-CDH4-2	CAAGGCUGGGUUCUCUGAAGTT
si-NC	UUCUCCGAACGUGUCACGUTT
sh-CDH4	GGACACAAUAUGAGACCAACA
sh-NC	UUCUCCGAACGUGUCACGU

Table S2 Antibodies used in this study.

Name	Company	Host	Catalog Number	dilution	Applications
CDH4	Bioworld	Mouse	MB62763	1:1000	WB
				1:50	IF
				1: 400	IHC
E-cadherin	Proteintech	Mouse	60335-1-Ig	1:4000	WB
				1:10000	IHC
GAPDH	Proteintech	Mouse	60004-1-Ig	1:50000	WB
α -Tublin	Proteintech	Mouse	66031-1-Ig	1:10000	WB
Histone H3	Beyotime	Mouse	AF0009	1:1000	WB
Na ⁺ /K ⁺ ATPase	abcam	Rabbit	ab76020	1:50000	WB
CD31	Beyotime	Rabbit	AG2849	1:400	IHC
β -catenin	Proteintech	Rabbit	51067-2-AP	1:4000	WB
				1:200	IF
Active β -catenin	abcam	Rabbit	ab246504	1:1000	WB
				1:100	IF
β -TrCP	Proteintech	Rabbit	28393-1-AP	1:1000	WB
VEGF-C	Beyotime	Rabbit	AF8325	1:1000	WB
c-Myc	Proteintech	Mouse	67447-1-Ig	1:2000	WB
				1:500	IHC
MMP7	Proteintech	Rabbit	10374-2-AP	1:1000	WB
				1:100	IHC

Table S3 Cellular location of CDH4 in PTC tissues according to clinicopathological information.

Characteristic	Number	CDH4 Location		<i>P</i> -values*
		CM	CP	
Age (years)				
≤ 55	36	10	26	0.99
> 55	10	3	7	
Sex				
Male	13	5	8	0.335
Female	33	8	25	
TNM stage				
I	42	13	29	0.464
II	4	0	4	
T stage				
T1a	19	6	13	0.824
T1b	21	5	16	
T2/3	6	2	4	
N stage				
Absent	23	6	17	0.743
Present	23	7	16	

* *P* values were calculated using the chi-square test.