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## Supplemental information

## ICAM1 antibody drug conjugates exert potent antitumor

#### activity in papillary and anaplastic thyroid carcinoma

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**Figure S1. Identification of DEGs in 3 PTC datasets according to GEO. Related to Figure 1.** (A) Volcano plots of the differential expression analysis for GSE3467, GSE33630 and GSE50901; (B) protein-protein interaction (PPI) analysis of DEGs performed by STRING; (C) identified hub gene by Cytoscape with different methods.



Figure S2. ICAM1 is overexpressed in ATC samples. Related to Figure 1. (A) Volcano plots of the differential expression analysis for GSE33630, GSE53072 and GSE65144; (B) mRNA level of ICAM1 in ATC compared with normal thyroid tissue; (C) ICAM1 mRNA level in ATC samples was significantly high than PTC and normal thyroid in GSE33630. Students' T test was employed in supplement figures 2C; \* p<0.05; \*\*\* p <0.001.



В

	adj.P.Val	P.Value	t	logFC
GSE33630	3.36e-11	2.39e-12	8.8877794	2.24481653
GSE53072	4.23e-03	3.02e-04	5.5101056	2.0282374
GSE65144	5.63e-04	3.07e-05	5.0460477	2.0361119



Figure S3. ICAM1-ADCs eradicate PTC and ATC tumors *in vivo*. Related to Figure 6. (A) Image of excised subcutaneous IHH4; (B) Image of excised subcutaneous 8505C; (C) H&E staining of main organs, including heart, lung, liver, spleen and kidney in ICAM1 antibody and paclitaxel group, scale bar equals to 20 µm; (H) blood chemistry parameters (TB and BUN) measured when treated mice were sacrificed in different groups.



# Table S1. Top10 hub gene by Cytoscape with different methods. Related to Figure

## 1.

Genes	MCC	Genes	EPC	Genes	MNC	Genes	DMNC	Genes	Degree
	Score		Score		Score		Score		Score
ICAM1	5	ICAM1	7.313	ICAM1	2	ICAM1	0.31	ICAM1	5
APOE	5	APOE	7.133	NCAM	2	KIT	0.31	APOE	5
SDC4	5	SDC4	6.941		2	ALOX5	0.31	SDC4	5
PUNY2	1	KIT	6 5 5 8	APOE	2	APOE	0.31	PUNY2	3
COMP			6.526	KIT	2	NCAM	0.31	COMP	4
COMP	5	KUNA2	0.330	KI I	2	1	0.51	COMP	5
KIT	3	NCAM	6.342	CSGAL	1	CSGAL	0	KIT	3
		1		NACT1		NACT1			
NCAM	3	COMP	6.167	ELMO1	1	ELMO1	0	NCAM	3
1								1	
TIAM1	2	ALOX5	6.002	TIAM1	1	TIAM1	0	TIAM1	2
TNFRS	2	TNFRS	5.824	GHR	1	GHR	0	TNFRS	2
F11B		F11B						F11B	
AGR2	2	TNC	5.746	TNFRS	1	TNFRS	0	AGR2	2
				F11B		F11B			
Genes	EcCent	Genes	Closene	Genes	Radiali	Genes	Stress	Genes	Betwee
	ricity		ss Score		ty Score		Score		nness
	ricity Score		ss Score		ty Score		Score		nness Score
СОМР	ricity Score 0.24	SDC4	ss Score	SDC4	ty Score 3.18	SDC4	<b>Score</b> 152	SDC4	nness Score 118.33
COMP SDC4	ricity           Score           0.24           0.24	SDC4 APOE	<b>ss Score</b> 10 9.75	SDC4 APOE	ty Score 3.18 3.098	SDC4 APOE	<b>Score</b> 152 116	SDC4 APOE	<b>nness</b> Score 118.33 87
COMP SDC4 CSGAL	ricity           Score           0.24           0.24           0.18	SDC4 APOE ICAM1	ss Score 10 9.75 9.33	SDC4 APOE COMP	ty Score 3.18 3.098 2.96	SDC4 APOE RUNX2	Score 152 116 86	SDC4 APOE COMP	nness           Score           118.33           87           58.66
COMP SDC4 CSGAL NACT1	ricity           Score           0.24           0.24           0.18	SDC4 APOE ICAM1	<b>ss Score</b> 10 9.75 9.33	SDC4 APOE COMP	ty Score 3.18 3.098 2.96	SDC4 APOE RUNX2	Score 152 116 86	SDC4 APOE COMP	nness         Score           118.33         87           58.66
COMP SDC4 CSGAL NACT1 TIAM1	ricity Score 0.24 0.24 0.18 0.18	SDC4 APOE ICAM1 COMP	ss Score 10 9.75 9.33 8.5	SDC4 APOE COMP ICAM1	ty Score 3.18 3.098 2.96 2.96	SDC4 APOE RUNX2 COMP	Score 152 116 86 84	SDC4 APOE COMP RUNX2	nness         Score           118.33         87           58.66         50.33
COMP SDC4 CSGAL NACT1 TIAM1 ADAM	ricity Score 0.24 0.24 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2	ss Score           10           9.75           9.33           8.5           8.41	SDC4 APOE COMP ICAM1 NCAM	ty Score 3.18 3.098 2.96 2.96 2.78	SDC4 APOE RUNX2 COMP ICAM1	Score 152 116 86 84 80	SDC4 APOE COMP RUNX2 ICAM1	nness           Score           118.33           87           58.66           50.33           48.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9	ricity Score 0.24 0.24 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2	ss Score           10           9.75           9.33           8.5           8.41	SDC4 APOE COMP ICAM1 NCAM 1	ty Score 3.18 3.098 2.96 2.96 2.78	SDC4 APOE RUNX2 COMP ICAM1	Score           152           116           86           84           80	SDC4 APOE COMP RUNX2 ICAM1	nness         Score           118.33         87           58.66         50.33           48.66         48.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT	ss Score           10           9.75           9.33           8.5           8.41           8.03	SDC4 APOE COMP ICAM1 NCAM 1 TNC	ty Score 3.18 3.098 2.96 2.96 2.78 2.78	SDC4 APOE RUNX2 COMP ICAM1 TIAM1	Score           152           116           86           84           80           36	SDC4 APOE COMP RUNX2 ICAM1 TIAM1	nness         Score           118.33         87           58.66         50.33           48.66         30
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1	ricity           Score           0.24           0.24           0.18           0.18           0.18           0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT	ss Score           10           9.75           9.33           8.5           8.41           8.03	SDC4 APOE COMP ICAM1 NCAM 1 TNC	ty Score 3.18 3.098 2.96 2.96 2.78 2.78	SDC4 APOE RUNX2 COMP ICAM1 TIAM1	Score           152           116           86           84           80           36	SDC4 APOE COMP RUNX2 ICAM1 TIAM1	nness         Score           118.33         87           58.66         50.33           48.66         30
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1	ss Score           10           9.75           9.33           8.5           8.41           8.03           8	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2	ty Score           3.18           3.098           2.96           2.96           2.78           2.789           2.78	SDC4 APOE RUNX2 COMP ICAM1 TIAM1 KIT	Score           152           116           86           84           80           36           36	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         17.33
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC ALOX5	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1 TNC	ss Score           10           9.75           9.33           8.5           8.41           8.03           8           7.58	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2 KIT	ty Score 3.18 3.098 2.96 2.96 2.78 2.78 2.789 2.78	SDC4 APOE RUNX2 COMP ICAM1 TIAM1 KIT TNFRS	Score           152           116           86           84           80           36           24	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT TNC	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         12.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC ALOX5	ricity         Score           0.24         0.24           0.18         0.18           0.18         0.18           0.18         0.18           0.18         0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1 TNC	ss Score           10           9.75           9.33           8.5           8.41           8.03           8           7.58	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2 KIT	ty Score           3.18           3.098           2.96           2.96           2.78           2.789           2.78           2.74	SDC4 APOE RUNX2 COMP ICAM1 TIAM1 KIT KIT TNFRS F11B	Score           152           116           86           84           80           36           24	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT TNC	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         12.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC ALOX5 APOE	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1 TNC ALOX5	ss Score           10           9.75           9.33           8.5           8.41           8.03           8           7.58           7.41	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2 KIT ALOX5	ty Score           3.18           3.098           2.96           2.96           2.78           2.78           2.78           2.74	SDC4 APOE RUNX2 COMP ICAM1 TIAM1 KIT KIT TNFRS F11B NCAM	Score           152           116           86           84           80           36           36           24           20	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT TNC NCAM	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         12.66           11.66         11.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC ALOX5 APOE	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1 TNC ALOX5	ss Score           10           9.75           9.33           8.5           8.41           8.03           8           7.58           7.41	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2 KIT ALOX5	ty Score           3.18           3.098           2.96           2.96           2.78           2.789           2.78           2.74	SDC4 APOE RUNX2 COMP ICAM1 TIAM1 KIT KIT TNFRS F11B NCAM 1	Score           152           116           86           84           80           36           24           20	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT TNC NCAM 1	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         12.66           11.66         11.66
COMP SDC4 CSGAL NACT1 TIAM1 ADAM TS9 NCAM 1 TNC ALOX5 APOE ICAM1	ricity Score 0.24 0.24 0.18 0.18 0.18 0.18 0.18 0.18 0.18 0.18	SDC4 APOE ICAM1 COMP RUNX2 KIT NCAM 1 TNC ALOX5 TNFRS	ss Score           10           9.75           9.33           8.5           8.41           8.03           8           7.58           7.41           7.36	SDC4 APOE COMP ICAM1 NCAM 1 TNC RUNX2 KIT ALOX5 TNFRS	ty Score           3.18           3.098           2.96           2.96           2.78           2.78           2.78           2.74           2.70           2.65	SDC4 APOE RUNX2 COMP ICAM1 ICAM1 TIAM1 KIT TNFRS F11B NCAM 1 TNC	Score           152           116           86           84           80           36           24           20           20	SDC4 APOE COMP RUNX2 ICAM1 TIAM1 KIT TNC NCAM 1 TNFRS	nness         Score           118.33         87           58.66         50.33           48.66         30           17.33         12.66           11.66         9.33

Table S2. Gene list of thyroid differentiation score and MAPK pathway activity

Thyroid differentiation score		MAPK pathway activity score		
Gene symbol	Gene full name	Gene symbol	Gene full name	
DIO1	iodothyronine deiodinase 1	SPRY2	sprouty RTK signaling antagonist 2	
DIO2	iodothyronine deiodinase 2	SPRY4	sprouty RTK signaling antagonist 4	
DUOX1	dual oxidase 1	ETV4	ETS variant transcription factor 4	
DUOX2	dual oxidase 2	ETV5	ETS variant transcription factor 5	
FOXE1	forkhead box E1	DUSP4	dual specificity phosphatase 4	
GLIS3	GLIS family zinc finger 3	DUSP6	dual specificity phosphatase 6	
NKX2-1	NK2 homeobox 1	CCND1	cyclin D1	
PAX8	paired box 8	EPHA2	EPH receptor A2	
SLC26A4	solute carrier family 26 member 4	EPHA4	EPH receptor A4	
SLC5A5	solute carrier family 5 member 5			
SLC5A8	solute carrier family 5 member 8			
TG	thyroglobulin			
THRA	thyroid hormone receptor alpha			
THRB	thyroid hormone receptor beta			
ТРО	thyroid peroxidase			
TSHR	thyroid stimulating hormone receptor			

score. Related to Figure 1.

Table S3. Top 5 most overexpressed antigens in unbiased screening of thyroid

PTC cell line		ATC cell line		
BCPAP	IHH4	8505C	TCO1	
ICAM1	ICAM1	ICAM1	PD-L1	
PD-L1	PD-L1	PD-L1	ICAM1	
ROR1	MUC-1	CXCR4	TROP2	
MUC-1	VEGFR2	ROR1	MUC-1	
VEGFR2	TROP2	TROP2	CD66a	

cancer-related antigens on PTC and ATC cells. Related to Figure 2.