

Supplementary Table 1: Primers and siRNA sequences

Target	Type	Location Within mRNA	SiRNA/Primer Name	Strand	Primer Sequence
<i>I. scapularis</i> <i>Vamp33</i>	siRNA	Start at 300	Vamp33SiF	Forward	AAGGACACAGTGTGGAGAGATCCTGTCTC
			Vamp33SiR	Reverse	AAATCTCTCCACACTGTGTCCCCTGTCTC
	Scrambled		Vamp33ScF	Forward	AAGTGAGGGACGCATAGTAGACCTGTCTC
			Vamp33ScR	Reverse	AATCTACTATGCGTCCCTCACCCCTGTCTC
	qRT-PCR	Start at 76	Vamp33qR-F	Forward	TCATACCTGAAGTTGTCCAA
		Start at 180	Vamp33qR-R	Reverse	CTCAAGAATGCCACTGTTG
<i>D. variabilis</i> <i>Vamp33</i>	siRNA	Start at 280	Vamp33Derm-SiF	Forward	AACCGGATGGTGATGTTAATCCCTGTCTC
			Vamp33Derm-SiR	Reverse	AAGATTAACATCACCATCCGGCCTGTCTC
	Scrambled		Vamp33Derm-ScF	Forward	AAGCCTCAGGTGGAATTAGTTCCTGTCTC
			Vamp33Derm-ScR	Reverse	AAAATAATTCCACCTGAGGCCCTGTCTC
	qRT-PCR	Start at 78	Vamp33DqR-2F	Forward	TCACCTAAAGTTGTCCAACCC
		Start at 160	Vamp33DqR-2R	Reverse	TCAAGGATTCCACTGTTGGG
	qRT-PCR	Start at 64	Vamp33DqR-F	Forward	GACGTGGTTACTTCTCACCTAAA
Start at 148		Vamp33DqR-R	Reverse	CTGTTGGGCCGTACACAATA	
<i>A. americanum</i> <i>Vamp33</i>	siRNA	Start at 280	Vamp33AA-SiF	Forward	AACCAGATGGTGATGTGAACCCCTGTCTC
			Vamp33AA-SiR	Reverse	AAGGTTACATCACCATCTGGCCTGTCTC
	Scrambled		Vamp33AA-ScF	Forward	AAGGGTGCTAACACGGACTTACCTGTCTC
			Vamp33AA-ScR	Reverse	AATAAGTCCGTGTTAGCACCCCTGTCTC
	qRT-PCR	Start at 76	Vamp33AA qR-F	Forward	TCTCATCTAAAGCTTTCCAACCC
		Start at 160	Vamp33AA qR-R	Reverse	AAGGATGCCACTGTTGGG
<i>I. scapularis</i> β -actin	qRT-PCR	Start at 618	ActinIS 2F	Forward	GGTCATCACAATCGGCAAC
		Start at 742	ActinIS 2R	Reverse	ATGGAGTTGTACGTGGTCTC
<i>A. americanum</i> β -actin	qRT-PCR	Start at 285	ActinAA F	Forward	GTCATGGTCGGCATGGG
		Start at 365	ActinAA R	Reverse	ATGCCGTGCTCAATGGG
<i>D. variabilis</i> β -actin	qRT-PCR	Start at 798	ActinIS 2F	Forward	GGTCATCACAATCGGCAAC
		Start at 905	ActinIS 2R	Reverse	ATGGAGTTGTACGTGGTCTC

Supplementary Table 2: Cell markers

Cell type	Cell population	Gene	Ensembl
Antigen presenting cells	All	<i>H2-Aa</i>	ENSMUSG00000036594
		<i>H2-Ab1</i>	ENSMUSG00000073421
	Langerhans	<i>Cd207</i>	ENSMUSG00000034783
	Dendritic cells	<i>Ilgax</i>	ENSMUSG00000030789
		<i>Cd80</i>	ENSMUSG00000075122
		<i>Cd86</i>	ENSMUSG00000022901
		<i>Ly75</i>	ENSMUSG00000026980
	Macrophage	<i>Cd209a</i>	ENSMUSG00000031494
		<i>Adgre1</i>	ENSMUSG00000004730
	Keratinocytes	Undifferentiated (Stratum basale)	<i>Ilgam</i>
<i>Krt5</i>			ENSMUSG00000061527
<i>Krt14</i>			ENSMUSG00000045545
Differentiating (Stratum spinosum)		<i>Krt15</i>	ENSMUSG00000054146
		<i>Krt 1</i>	ENSMUSG00000046834
		<i>Krt2</i>	ENSMUSG00000064201
Terminally differentiated (Stratum granulosum)		<i>Krt10</i>	ENSMUSG00000019761
		<i>Ivl</i>	ENSMUSG00000049128
Corneocytes (Stratum corneum)		<i>Flg</i>	ENSMUSG00000102439
T cells		All	<i>Klk5</i>
	<i>Cd3d</i>		ENSMUSG00000032094
	<i>Cd3e</i>		ENSMUSG00000032093
	$\alpha\beta$ T cell	<i>Cd3g</i>	ENSMUSG00000002033
		<i>Trac</i>	ENSMUSG00000076928
		<i>Trbc1</i>	ENSMUSG00000076490

		<i>Trbc2</i>	ENSMUSG00000076498
		<i>CD4</i>	ENSMUSG00000023274
		<i>CD8a</i>	ENSMUSG00000053977
	γδ T cell	<i>Trdc</i>	ENSMUSG00000104876
		<i>Tcrg-C1</i>	ENSMUSG00000076749
		<i>Tcrg-C2</i>	ENSMUSG00000076752
		<i>Tcrg-C4</i>	ENSMUSG00000076757
	DETCs	<i>Trdv4</i>	ENSMUSG00000076867
		<i>Sema4d</i>	ENSMUSG00000021451
		<i>Jaml</i>	ENSMUSG00000048534
		<i>Klrk1</i>	ENSMUSG00000030149
Endothelial		<i>Cldn5</i>	ENSMUSG00000041378
		<i>Cdh5</i>	ENSMUSG00000031871
		<i>Egfl7</i>	ENSMUSG00000026921
Fibroblasts		<i>Dcn</i>	ENSMUSG00000019929
		<i>Fgf2</i>	ENSMUSG00000037225
		<i>Fgf7</i>	ENSMUSG00000027208
Hair follicle	Upper hair follicle	<i>Krt79</i>	ENSMUSG00000061397
		<i>Krt17</i>	ENSMUSG00000035557
	Sebaceous gland	<i>Mgst1</i>	ENSMUSG00000008540
		<i>Scd1</i>	ENSMUSG00000037071
	Outer bulge	<i>Postn</i>	ENSMUSG00000027750
		<i>Lgr5</i>	ENSMUSG00000020140
	Inner bulge	<i>Krt6a</i>	ENSMUSG00000058354
		<i>Krt75</i>	ENSMUSG00000022986
Base of follicle	<i>Shh</i>	ENSMUSG00000002633	
Hair germ	<i>Gli1</i>	ENSMUSG00000025407	
Melanocytes		<i>Dct</i>	ENSMUSG00000022129

		<i>Mlana</i>	ENSMUSG00000024806
		<i>Tyr</i>	ENSMUSG00000004651
Red blood cells		<i>Hbb-bs</i>	ENSMUSG00000052305
		<i>Hbb-bt</i>	ENSMUSG00000073940
Schwann cells		<i>Mal</i>	ENSMUSG00000027375
		<i>Plp1</i>	ENSMUSG00000031425
		<i>Sox10</i>	ENSMUSG00000033006
Smooth muscle cells		<i>Acta2</i>	ENSMUSG00000035783
		<i>Myh11</i>	ENSMUSG00000018830
		<i>Myl9</i>	ENSMUSG00000067818
		<i>Myocd</i>	ENSMUSG00000067818
		<i>Rgs5</i>	ENSMUSG00000026678

1073

Supplementary Table 3: Resources and reagents available

Antibody	Source	Identifier	Dilution/ Concentration
7-AAD Viability Staining Solution	Biolegend	420404	1:500
Zombie Violet Fixable Live Dead stain	Biolegend	423113	1:500
Zombie NIR Fixable Live Dead stain	Biolegend	423105	1:500
Anti-mouse CD16/32 Antibody	Biolegend	156603	1:500
APC anti-mouse CD45 Antibody clone: 30-F11	Biolegend	103111	1:100
FITC anti-mouse CD3 Antibody clone:17A2	Biolegend	100203	1:100
BV650 anti-mouse Vy3 Antibody clone: 536	BD	743241	1:50
PE Mouse Anti-Rat IgM clone:G53-238	BD	553888	1:100
Monoclonal antibody 17D1	Adrian Hayday, Kings College London and Robert Tigelaar, Yale University	N/A	1:50
PE/Cyanine7 anti-mouse CD45 Antibody clone: 30-F11	Biolegend	103114	1:100
APC anti-mouse Thy1.2 Antibody clone: 30-H12	Biolegend	105312	1:100
PE anti-mouse JAML Antibody clone: 4E10	Biolegend	128503	1:100
BV711 anti-mouse CD100 Antibody clone: BMA-12	BD	745492	1:100
PE/Cyanine5 anti-mouse CD44 Antibody clone: IM7	Biolegend	103010	1:100
APC/Cyanine7 anti-mouse CD25 Antibody clone: PC61	Biolegend	102026	1:100
PerCP/Cyanine5.5 anti-mouse CD69 Antibody clone: H1.2F3	Biolegend	104522	1:100
APC anti-mouse CD314 (NKG2D) Antibody clone: CX5	Biolegend	130212	1:100
Alexa Fluor 700 anti-mouse Ki-67 Antibody clone: 16A8	Biolegend	652420	1:50
BV711 anti-mouse CD326 (Ep-CAM) Antibody clone: G8.8	Biolegend	118233	1:100
PE anti-mouse CD200 Antibody clone: OX-90	Biolegend	123807	1:100
PE/Cyanine5 anti-mouse CD34 Antibody clone: MEC14.7	Biolegend	119312	1:100
BV605 anti-mouse Sca1 Antibody clone: D7	Biolegend	108133	1:100

PE anti-mouse CD49f Antibody clone: GoH3	Biolegend	313612	1:100
FITC Phospho-PI3K p85/p55 (Tyr458, Tyr199) Monoclonal Antibody clone: PI3KY458-1A11	ThermoFisher Scientific	MA5-36955	1:50
PI3K p85 α Monoclonal Antibody clone: SU04-07	ThermoFisher Scientific	MA5-41128	1:50
Alexa Fluor 405 Goat anti-Rabbit IgG (H+L) Secondary Antibody	ThermoFisher Scientific	A-31556	1:100
Anti-MADH7/SMAD7 polyclonal antibody	Abcam	ab216428	1:100

Cell media			
Leibovitz's L-15 Medium, powder	Gibco	41300039	N/A
L-aspartic acid	Millipore-Sigma	11189	0.449 g/L
L-glutamine	Millipore-Sigma	G8540	0.500 g/L
L-proline	Millipore-Sigma	81709	0.450 g/L
L-glutamic acid	Millipore-Sigma	49449	0.250 g/L
α -ketoglutaric acid	Millipore-Sigma	K1128	0.449 g/L
Sodium hydroxide	Millipore-Sigma	S8045	10 N
D-glucose	Millipore-Sigma	G7021	18.018 g/L
FBS (USDA approved; for tick media)	Millipore-Sigma	F0926-500ML	0.1
Bacto™ Tryptose Phosphate Broth	BD	260300	5%
Lipoprotein Concentrate	MP Biomedicals	191476	0.1%
Corning® 100 mL Penicillin-Streptomycin Solution, 100x	Corning	30-002-CI	1:100
Amphotericin B	Gibco	15290-026	1:100
Distilled water	Gibco	15-230-147	N/A
Materials			
Cell culture plate with lid (6 well, flat bottom)	Sigma	SIAL0516	N/A

Cellstart®, 96 well cell culture plate, F-bottom	Greiner bio-one	655 160	N/A
Costar® cell culture plate with lid (24 well, flat bottom)	Corning	CLS3526-1EA	N/A
Nunc™ 96-Well Polystyrene Round Bottom Microwell Plates	Thermo Scientific	262162	N/A
Vannas spring scissors, 4 mm cutting edge straight	Fine Science	15018-10	N/A
Integra Miltex 2 mm biopsy punches	Integra	95039-098	N/A
Integra Miltex 5 mm biopsy punches	Integra	33-35	N/A
AcuPunch biopsy punches 10 mm	Acuderm	P1050	N/A
FALCON® 14 ml Polypropylene round-bottom tube	Corning	352059	N/A
Corning® cell strainer size 40 µm, blue, sterile	Corning	431750	N/A
Falcon 5 mL Round Bottom Polystyrene Test Tube, with Cell Strainer Snap Cap	Corning	352235	N/A
12x75mm Plastic Tubes	Globe Scientific	110441	N/A
1.5 mL Eppendorf Safe-Lock Tubes	USA Scientific	1615-5500	N/A
1.5ml Microcentrifuge Tubes with Socket Screw Caps	VWR	525-1238	N/A
Lo-bind tubes	Eppendorf	22431048	N/A
Vannas Spring Scissors - 4mm	Fine Science Tools	15018-10	N/A
Reagents			
Trypsin/Lys-C Mix, Mass Spec Grade	Promega	V5071	N/A
Bovine Serum Albumin	Millipore-Sigma	A2058-5G	N/A
BenchMark™ FBS	Gemini Bio-products	100-106	1:10
Methanol anhydrous, 99.8%	Millipore-Sigma	322415-1L	0-20%
Ethyl alcohol, Pure; 200 proof for molecular biology	Millipore-Sigma	E7023-1L	1:1
TRIzol reagent	Ambion	15596018	N/A
Liberase™ TL Research Grade	Roche	540102000 1	10%
RPMI-1640 with L-Glutamine	Quality Biological	722461	N/A

DNase I	Roche	112849320 01	N/A
10X Phosphate-buffered saline (PBS)	Quality Biological	119-069- 131	1X
Phosphate-buffered saline (PBS)	Gibco	10010-023	N/A
0.5M Ethylenediaminetetraacetic acid (EDTA), pH 8.0	Boston BioProducts	BM-150	N/A
Sodium azide (NaN ₃)	Sigma-Aldrich	S2002-25G	N/A
Paraformaldehyde	Thermo Fisher Scientific	J61899-AP	N/A
RIPA lysis buffer	Millipore	20-188	1X
Halt Protease Inhibitor Cocktail	Thermo Fisher Scientific	87786	1X
Halt™ Phosphatase Inhibitor Cocktail	Thermo Fisher Scientific	78420	1X
Dispase II	Sigma-Aldrich	D4693-1G	NA
Dispase	Gibco	17105-041	4 U/mL
Magnesium chloride (MgCl ₂)	Sigma-Aldrich	M2393- 100G	5mM
Calcium chloride (CaCl ₂)	Sigma-Aldrich	C1016- 100G	0.4mM
Collagenase D	Sigma-Aldrich	110888660 01	2.5mg/mL
Gum rosin	Millipore-Sigma	60895	75% (3/4 parts)
Beeswax	Thermo Fisher Scientific	S25192A	25% (1/4 parts)
Cytochalasin D	Sigma-Aldrich	C8273	1:100
Commercial Assays			
Pure Link RNA mini kit	Ambion	12183025	N/A
Silencer™ siRNA Construction Kit	Thermo Scientific	AM1620	N/A
Verso cDNA Synthesis Kit	Thermo Scientific	AB-1453B	N/A
Pierce BCA Protein Assay Kit	Thermo Scientific	23227	N/A
DNeasy® Blood and Tissue kit	Qiagen	69506	N/A

FOXP3 Fix/Perm Buffer Set	BioLegend	421403	N/A
Human KGF/FGF-7 Quantikine ELISA Kit	R&D Systems	DKG00	NA
Human/Mouse/Rat/Porcine/Canine TGF- β 1 ELISA – Quantikine kit	R&D Systems	DB100C	NA
Organisms			
<i>Ixodes scapularis</i> adult partially fed female ticks	Albert Mulenga, Texas A&M University	N/A	N/A
<i>Ixodes scapularis</i> adult partially fed female ticks	Adela Oliva Chavez, Texas A&M University	N/A	N/A
<i>Ixodes scapularis</i> nymph ticks	Jon Oliver and Ulrike Munderloh, University of Minnesota	N/A	N/A
<i>Ixodes scapularis</i> nymph ticks	Tick Lab, Oklahoma State University	N/A	N/A
<i>Amblyomma americanum</i> nymph ticks	Tick Lab, Oklahoma State University	N/A	N/A
<i>Dermacentor variabilis</i> nymph ticks	Tick Lab, Oklahoma State University	N/A	N/A
C57BL6J (WT) mice	University of Maryland	N/A	N/A
C57BL6J (WT) mice	Jackson Laboratories	#000664	N/A
FVB/NJ mice	The Jackson Laboratory	001800	N/A
FVB/NTac mice	Taconic Biosciences	N/A	N/A
Equipment			
CFX96 Touch Real-Time PCR Detection System	Biorad	N/A	N/A
Nanoject III	Drummond Scientific Company	3-000-207	N/A
NanoSight NS300	Malvern Panalytical	N/A	N/A
Percival I30BLL incubator	Percival	I30BLL	N/A
Software			
GraphPad Prism v9.1.2	https://www.graphpad.com/	N/A	N/A
GraphPad Quick Cals Outlier Calculator	https://www.graphpad.com/quickcalcs/Gru/bbs1.cfm	N/A	N/A

FlowJo (v10.6.1 – 10.8.1)	https://www.flowjo.com/	N/A	N/A
QIAGEN Ingenuity Pathway Analysis	https://digitalinsights.qiagen.com/products-overview/discovery-insights-portfolio/analysis-and-visualization/qiagen-ipa/	N/A	N/A
Database for Annotation, Visualization and Integrated Discovery (DAVID) (version 2021)	https://david.ncifcrf.gov/	N/A	N/A

1075

1076