

Supporting Information

Novel role of ASH1L histone methyltransferase in anaplastic thyroid carcinoma

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Materials Included:

Figure S1. The growth of ATC cell line BHT-101 is dependent on ASH1L expression.

Figure S2. The growth of ATC cell lines SW1736 and JEM493 is dependent on ASH1L.

Table S1. Differentially expressed genes, sorted by FDR, in ASH1L knockout BHT-101 cells compared to wild type BHT-101 cells.

Table S2. Enriched gene sets, sorted by FDR, in ASH1L knockout BHT-101 cells compared to wild type BHT-101 cells.

Table S3 is provided separately as an xlsx file. H3K36me2 ChIP-seq peaks present in BHT-101 wild type cells but absent in ASH1L knockout clones 1 and 4, and annotated to the differentially expressed genes in Figure 3 and Table S1.

Table S4. Real time PCR primers for human gene expression studies.

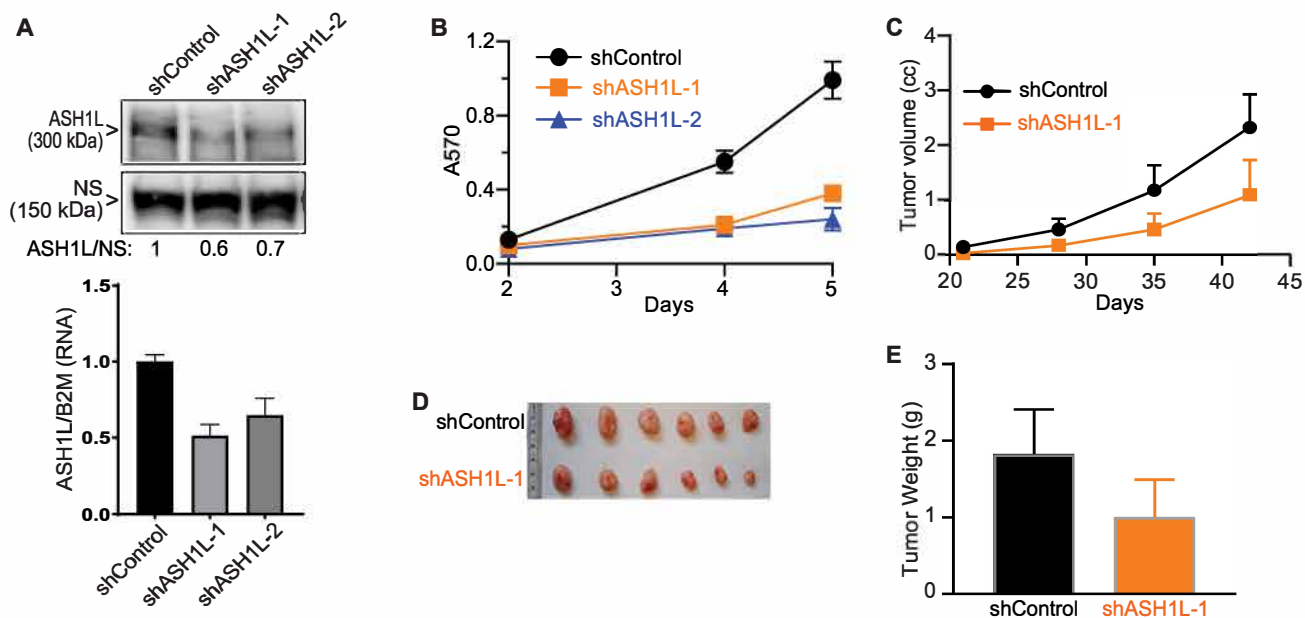


Figure S1. The growth of ATC cell line BHT-101 is dependent on ASH1L expression. *A, upper panel.* Western blot of ASH1L protein in BHT-101 cells expressing shControl or either of 2 shRNAs targeting ASH1L. The ASH1L band is 300 kDa. A non-specific band (NS, 150 kDa) serves as a loading control. *A, lower panel.* ASH1L mRNA expression analyzed by RT-qPCR and normalized to beta-2 microglobulin (B2M). *B.* MTT assay of BHT-101 shControl versus shASH1L cells. Data points are the mean \pm SD of sextuplet culture wells. Both shASH1L cell lines differ from shControl on days 4 and 5, $p < 0.0001$, Dunnett's test. *C.* BHT-101 shControl or shASH1L-1 cells were injected into the flanks of NOD-SCID mice, 5×10^6 cells per injection and tumor volumes were estimated with calipers. Data points are the mean \pm SD of 6 mice per cell line. At each time point, shASH1L differs from shControl, $p < 0.02$, t test with Holm-Sidak correction for multiple comparisons. *D.* The mice from panel C were sacrificed 42 days post-injection and the tumors were harvested. *E.* Tumor weights from panel D, mean \pm SD. The shASH1L tumors weigh less than shControl, $p = 0.025$, 2-tailed t test.

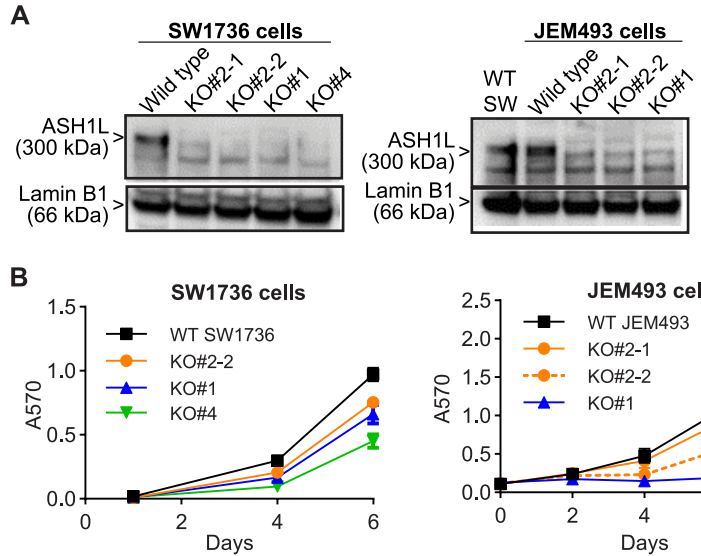


Figure S2. The growth of ATC cell lines SW1736 and JEM493 is dependent on ASH1L. **A.** ASH1L protein expression was knocked out of SW1736 cells using CRISPR-Cas9 and gRNAs 1, 2 and 4 from the BHT-101 cell knockout procedure, and was similarly knocked out of JEM493 cells using gRNAs 1 and 2. For each cell line, two independent clones were isolated using gRNA 2, denoted 2-1 and 2-2. Western blots of nuclear extracts confirm loss of ASH1L protein. The ASH1L band is 300 kDa, and Lamin B1 (66 kDa) is used as a loading control. A faint band in almost exactly the same position as ASH1L is detected in SW1736 KO cell line 2-1. The identity of this band is not known, and this cell line was not studied further. The first lane of the JEM493 Western blot is from wild type SW1736 cells (WT SW), to confirm the position of ASH1L in the JEM493 cells. **B.** The SW1736 and JEM493 cell lines with ASH1L KO grow more slowly than wild type cells in culture, assessed by MTT assay. Each data point represents the mean \pm SD of sextuplicate wells. All KO lines are different than wild type at days 4 and beyond, $p < 0.001$, Dunnett's test, except JEM493 KO#2-1 is significant $p < 0.001$ only on day 8.

Table S1. Differentially expressed genes, sorted by FDR, in ASH1L knockout BHT-101 cells compared to wild type BHT-101 cells. Differentially expressed genes are defined as having FDR<0.05 and absolute fold change >2 in the same direction in all 4 knockout cell clones versus 3 separate passages of wild type cells, analyzed by RNA-seq. Ten genes also were analyzed by RT-qPCR to confirm the RNA-seq results, shown in the last column.

Gene symbol	Log ₂ Fold		<i>p</i> -Value	FDR	RT-qPCR
	Change	log ₂ CPM ^a			Log ₂ Fold Change
<i>SLC6A15</i>	-8.01	2.521	1.56E-43	2.04E-39	-7.79
<i>TSSC2</i>	-5.93	2.679	6.27E-26	4.12E-22	-2.60
<i>ONECUT3</i>	-5.27	0.313	5.04E-22	2.21E-18	-5.80
<i>RNF212</i>	3.31	3.069	8.54E-21	2.81E-17	
<i>AC091801.1</i>	8.04	1.038	1.81E-19	4.76E-16	
<i>SLC1A1</i>	3.12	3.660	3.71E-18	8.13E-15	
<i>GLB1L3</i>	-4.87	-0.129	3.30E-17	6.19E-14	
<i>INPP4B</i>	4.14	3.406	4.20E-14	6.90E-11	
<i>PTCHD4</i>	5.81	1.401	1.10E-13	1.60E-10	
<i>HAPLN1</i>	-5.08	3.313	1.34E-13	1.76E-10	-5.59
<i>NUP210</i>	1.58	7.340	2.71E-13	3.24E-10	
<i>VSTM2L</i>	-2.45	5.871	2.84E-12	3.11E-09	
<i>IGFBP7</i>	4.53	1.972	8.64E-11	7.18E-08	
<i>MORC4</i>	-2.14	5.514	8.74E-11	7.18E-08	
<i>LRRC6</i>	2.84	1.527	1.37E-10	1.06E-07	
<i>MMP16</i>	5.58	2.957	1.77E-10	1.30E-07	
<i>GLI3</i>	2.58	3.923	3.22E-10	2.23E-07	
<i>FBN1</i>	1.80	4.762	3.77E-10	2.48E-07	
<i>PRICKLE1</i>	5.76	3.756	1.82E-09	1.01E-06	
<i>ZNF827</i>	2.01	3.451	1.85E-09	1.01E-06	
<i>FADS2</i>	-1.62	7.141	4.92E-09	2.31E-06	
<i>LDOC1</i>	3.14	4.367	4.77E-09	2.31E-06	
<i>SPOCK1</i>	6.36	5.402	5.77E-09	2.62E-06	
<i>ANKRD1</i>	-2.10	5.449	6.94E-09	2.94E-06	
<i>SLC46A1</i>	1.90	3.595	8.13E-09	3.34E-06	
<i>COL4A2</i>	1.72	6.931	1.54E-08	6.12E-06	
<i>TEX15</i>	4.21	0.788	2.22E-08	8.57E-06	
<i>LAYN</i>	3.12	-0.098	3.14E-08	1.14E-05	
<i>ATP10D</i>	1.71	4.054	4.99E-08	1.73E-05	
<i>BMP4</i>	1.95	4.144	5.66E-08	1.91E-05	
<i>TOX2</i>	2.77	3.862	5.88E-08	1.92E-05	
<i>PRKCZ</i>	2.52	2.993	8.66E-08	2.65E-05	
<i>PTK7</i>	3.22	3.005	9.18E-08	2.74E-05	
<i>COL7A1</i>	1.86	6.419	1.17E-07	3.34E-05	
<i>STAC</i>	2.68	5.209	1.15E-07	3.34E-05	
<i>NRP2</i>	2.04	3.995	1.33E-07	3.65E-05	
<i>SCARA3</i>	-1.60	4.494	1.64E-07	4.30E-05	
<i>SHROOM2</i>	2.63	-0.252	1.98E-07	4.92E-05	
<i>ARHGAP10</i>	3.12	2.959	2.03E-07	4.95E-05	
<i>DFNA5</i>	2.39	3.184	2.16E-07	5.08E-05	
<i>STK32B</i>	4.63	2.971	2.94E-07	6.78E-05	
<i>CCAT1</i>	-6.10	2.245	3.32E-07	7.52E-05	-6.97
<i>NUDT11</i>	2.20	2.345	3.44E-07	7.67E-05	

<i>NNMT</i>	-2.88	5.768	4.07E-07	8.76E-05	-3.31
<i>AHRR</i>	2.62	3.323	4.49E-07	9.51E-05	
<i>AGPAT3</i>	2.23	4.088	5.01E-07	1.00E-04	
<i>FAM20C</i>	2.43	0.124	4.98E-07	1.00E-04	
<i>PEAR1</i>	-2.06	4.364	5.03E-07	1.00E-04	
<i>SMIM3</i>	3.54	0.126	4.93E-07	1.00E-04	
<i>SYT14</i>	5.51	1.260	7.18E-07	1.37E-04	
<i>GPNMB</i>	2.00	0.068	7.49E-07	1.40E-04	
<i>CCDC80</i>	2.32	0.672	1.09E-06	1.97E-04	
<i>FGF1</i>	2.92	1.048	1.12E-06	1.97E-04	
<i>GCNT1</i>	4.05	0.998	1.25E-06	2.16E-04	
<i>TWSG1</i>	-1.60	5.348	1.49E-06	2.48E-04	
<i>TRIB3</i>	-1.66	7.718	2.19E-06	3.60E-04	
<i>FZD2</i>	2.65	1.652	2.29E-06	3.72E-04	
<i>FAM49A</i>	2.28	0.525	2.38E-06	3.81E-04	
<i>ADGRB2</i>	1.63	2.121	2.88E-06	4.46E-04	
<i>COL12A1</i>	6.39	2.555	3.00E-06	4.48E-04	
<i>COL4A1</i>	1.96	5.957	2.99E-06	4.48E-04	
<i>CSAG1</i>	3.10	1.293	3.13E-06	4.62E-04	
<i>CD3D</i>	-4.74	2.005	3.25E-06	4.75E-04	
<i>FOXF1</i>	6.83	1.225	3.49E-06	4.98E-04	
<i>HLA-B</i>	3.40	-0.030	3.71E-06	5.25E-04	
<i>MAP7</i>	-1.72	0.690	4.13E-06	5.72E-04	
<i>ARAP2</i>	6.85	2.405	4.34E-06	5.82E-04	
<i>GAS6-AS1</i>	2.26	1.773	4.27E-06	5.82E-04	
<i>ZNF503</i>	1.84	0.768	4.45E-06	5.90E-04	
<i>HOXB8</i>	-1.89	0.969	4.74E-06	6.23E-04	
<i>SLC27A2</i>	2.41	0.788	5.91E-06	7.61E-04	
<i>LIMD2</i>	-1.41	3.626	6.07E-06	7.75E-04	
<i>RP11-115D19.1</i>	5.21	0.374	6.77E-06	8.47E-04	
<i>SNAI2</i>	2.17	4.158	7.43E-06	9.21E-04	
<i>NPTXR</i>	2.69	1.331	8.17E-06	0.0010	
<i>PCDH10</i>	6.63	1.578	8.48E-06	0.0010	
<i>CTB-1121.1</i>	4.14	0.404	8.82E-06	0.0011	
<i>COL5A1</i>	2.84	6.164	9.01E-06	0.0011	
<i>LINC01021</i>	2.56	3.114	9.54E-06	0.0011	
<i>AC002480.3</i>	-1.70	3.036	1.02E-05	0.0012	
<i>SAMD13</i>	1.85	-0.328	1.07E-05	0.0012	
<i>SDK1</i>	8.82	4.255	1.19E-05	0.0013	
<i>LINC00173</i>	-2.14	0.190	1.21E-05	0.0013	-2.39
<i>IL6</i>	-1.87	1.131	1.23E-05	0.0013	-1.74
<i>ADAMTS14</i>	8.02	0.276	1.24E-05	0.0013	
<i>ITPRIPL1</i>	-2.00	1.638	1.29E-05	0.0014	
<i>DTX3</i>	1.78	3.143	1.41E-05	0.0015	
<i>PCLO</i>	4.47	2.981	1.42E-05	0.0015	
<i>SOX9</i>	1.95	4.474	1.96E-05	0.0020	
<i>CPHLIP</i>	-3.75	3.645	2.04E-05	0.0021	
<i>CLMP</i>	3.57	0.927	2.15E-05	0.0022	
<i>RASD2</i>	3.02	0.904	2.19E-05	0.0022	
<i>COL21A1</i>	-2.31	0.517	2.26E-05	0.0022	
<i>SPECC1</i>	1.97	2.699	2.39E-05	0.0023	

<i>VGLL3</i>	-1.93	5.498	2.50E-05	0.0024	
<i>ARHGEF25</i>	1.60	1.055	2.62E-05	0.0024	
<i>NR2F1</i>	-1.64	4.760	2.61E-05	0.0024	
<i>CASC15</i>	-2.55	0.590	2.66E-05	0.0024	
<i>SUSD4</i>	4.40	0.385	3.06E-05	0.0028	
<i>ARSI</i>	3.88	0.083	3.11E-05	0.0028	
<i>BNC1</i>	5.43	1.659	3.33E-05	0.0029	
<i>DIRAS3</i>	5.03	0.175	3.33E-05	0.0029	
<i>FNDC10</i>	1.35	3.381	3.42E-05	0.0029	
<i>PPP1R14A</i>	-2.31	3.057	3.42E-05	0.0029	
<i>TRABD2A</i>	2.33	3.270	3.39E-05	0.0029	
<i>ANXA10</i>	2.88	1.147	3.70E-05	0.0031	
<i>LVCAT1</i>	2.07	0.265	3.74E-05	0.0032	
<i>NLRC5</i>	2.32	1.498	3.79E-05	0.0032	
<i>HMOX1</i>	-1.41	4.329	3.93E-05	0.0032	
<i>STARD13</i>	2.99	2.301	4.21E-05	0.0034	
<i>MBNL3</i>	1.75	2.863	4.63E-05	0.0038	
<i>MIR646HG</i>	-1.56	0.335	4.90E-05	0.0039	
<i>GOLGA7B</i>	-1.84	3.003	5.96E-05	0.0046	
<i>ADAM19</i>	2.43	3.638	6.11E-05	0.0047	
<i>LONRF2</i>	1.79	0.784	6.25E-05	0.0048	
<i>IGFBP1</i>	-2.31	3.822	7.28E-05	0.0055	
<i>IFI27L2</i>	2.48	-0.064	7.44E-05	0.0056	
<i>NAT8L</i>	2.76	1.054	7.44E-05	0.0056	
<i>NRGN</i>	-1.20	3.262	7.74E-05	0.0056	
<i>MAGEA12</i>	2.95	2.461	8.16E-05	0.0059	
<i>PRDM9</i>	-4.37	0.259	9.93E-05	0.0069	-0.68
<i>TRBC1</i>	-1.95	-0.037	1.08E-04	0.0074	
<i>CD9</i>	-1.42	7.016	1.09E-04	0.0074	
<i>NHSL2</i>	-2.78	3.826	1.35E-04	0.0088	
<i>NOV</i>	1.71	1.669	1.36E-04	0.0088	
<i>GAB1</i>	1.86	2.066	1.40E-04	0.0090	
<i>RP11-408N14.1</i>	-3.62	0.178	1.54E-04	0.0099	
<i>GRIK2</i>	2.54	1.349	1.56E-04	0.0099	
<i>CRYAB</i>	-1.55	1.114	1.74E-04	0.0107	
<i>RNF208</i>	1.44	1.513	1.74E-04	0.0107	
<i>SEMA6B</i>	2.01	2.051	1.72E-04	0.0107	
<i>NKILA</i>	3.28	0.864	2.12E-04	0.0124	
<i>PAX9</i>	-1.56	4.925	2.22E-04	0.0129	
<i>PNPLA3</i>	1.47	1.406	2.24E-04	0.0129	
<i>TUSC1</i>	2.03	2.974	2.25E-04	0.0129	
<i>LINC01929</i>	-3.60	-0.631	2.51E-04	0.0141	-3.47
<i>KCNAB3</i>	-1.38	-0.251	2.53E-04	0.0141	
<i>CLUHP3</i>	1.37	2.458	2.72E-04	0.0148	
<i>TLE4</i>	3.12	1.777	3.14E-04	0.0166	
<i>TRPA1</i>	-1.75	5.798	3.46E-04	0.0179	
<i>RP11-369E15.3</i>	-3.48	2.623	3.60E-04	0.0183	
<i>TMEM204</i>	-3.47	0.776	3.68E-04	0.0184	
<i>RP5-940J5.9</i>	-1.29	1.845	4.21E-04	0.0207	
<i>CDK14</i>	2.26	2.225	4.37E-04	0.0210	
<i>IPCEF1</i>	-1.86	0.596	4.66E-04	0.0220	

<i>ZSWIM5</i>	-2.12	3.183	5.99E-04	0.0253
<i>C9orf116</i>	1.13	2.377	6.19E-04	0.0258
<i>CAPS2</i>	1.19	1.498	6.26E-04	0.0260
<i>ITGB7</i>	-2.34	-0.034	8.42E-04	0.0319
<i>WNT6</i>	-1.47	-0.365	9.05E-04	0.0334
<i>ITGA11</i>	4.10	1.910	9.69E-04	0.0350
<i>ASNS</i>	-1.83	7.753	9.99E-04	0.0359
<i>RP11-64D22.5</i>	1.12	0.911	0.0011	0.0373
<i>MCC</i>	3.53	1.308	0.0012	0.0409
<i>CYP11A1</i>	3.14	1.392	0.0014	0.0438
<i>TTC9</i>	-1.73	3.390	0.0016	0.0494

^aCPM, counts per million.

Table S2. Enriched gene sets, sorted by FDR, in ASH1L knockout BHT-101 cells compared to wild type BHT-101 cells.

Id	Name	Concept Type	P-Value	FDR
GO:0030574	collagen catabolic process	GOBP	9.98E-09	3.16E-05
GO:0044243	multicellular organism catabolic process	GOBP	9.98E-09	3.16E-05
GO:0001764	neuron migration	GOBP	4.66E-08	7.38E-05
GO:0055114	oxidation-reduction process	GOBP	4.36E-08	7.38E-05
GO:0044236	multicellular organism metabolic process	GOBP	1.87E-07	1.48E-04
GO:0032963	collagen metabolic process	GOBP	3.01E-07	1.80E-04
GO:0044259	multicellular organismal macromolecule metabolic process	GOBP	2.97E-07	1.80E-04
GO:1903335	regulation of vacuolar transport	GOBP	3.43E-07	1.81E-04
GO:0006082	organic acid metabolic process	GOBP	1.04E-06	4.37E-04
GO:0044283	small molecule biosynthetic process	GOBP	1.38E-06	5.46E-04
GO:0030198	extracellular matrix organization	GOBP	4.82E-06	1.39E-03
GO:0043062	extracellular structure organization	GOBP	4.82E-06	1.39E-03
c7.immunologic.all.GSE13411_NAIVE_VS_MEMORY_BCELL_UP	c7.immunologic.all.GSE13411_NAIVE_VS_MEMORY_BCELL_UP	Custom	5.85E-07	1.92E-03
c7.immunologic.all.GSE37532_VISCERAL_ADIPOSE_TISSUE_VS_LN_DERIVED_PPARG_KO_TC0NV_CD4_TCELL_DN	c7.immunologic.all.GSE37532_VISCERAL_ADIPOSE_TISSUE_VS_LN_DERIVED_PPARG_KO_TCONV_CD4_TCELL_DN	Custom	7.91E-07	1.92E-03
c7.immunologic.all.GSE19825_NAIVE_VS_DAY3_EFF_CD8_TCELL_UP	c7.immunologic.all.GSE19825_NAIVE_VS_DAY3_EFF_CD8_TCELL_UP	Custom	1.03E-06	1.92E-03
GO:0010812	negative regulation of cell-substrate adhesion	GOBP	9.58E-06	2.33E-03
GO:0018205	peptidyl-lysine modification	GOBP	1.25E-05	2.77E-03
c7.immunologic.all.GSE22601_DOUBLE_NEGATIVE_VS_CD4_SINGLE_POSITIVE_THYMOCYTE_UP	c7.immunologic.all.GSE22601_DOUBLE_NEGATIVE_VS_CD4_SINGLE_POSITIVE_THYMOCYTE_UP	Custom	3.21E-06	4.48E-03
GO:0032787	monocarboxylic acid metabolic process	GOBP	2.89E-05	5.39E-03
GO:0035987	endodermal cell differentiation	GOBP	3.04E-05	5.50E-03
hallmark.all.HALLMARK_OXIDATIVE_PHOSPHORYLATION	hallmark.all.HALLMARK_OXIDATIVE_PHOSPHORYLATION	Custom	6.62E-06	7.40E-03
GO:1901657	glycosyl compound metabolic process	GOBP	5.03E-05	8.38E-03
GO:0042278	purine nucleoside metabolic process	GOBP	5.51E-05	8.63E-03
GO:0046128	purine ribonucleoside metabolic process	GOBP	5.51E-05	8.63E-03
GO:0019752	carboxylic acid metabolic process	GOBP	5.73E-05	8.63E-03

GO:0043436	oxoacid metabolic process	GOBP	5.73E-05	8.63E-03
GO:0006631	fatty acid metabolic process	GOBP	7.59E-05	9.77E-03
GO:0009116	nucleoside metabolic process	GOBP	8.12E-05	0.0101
c7.immunologic.all.GSE2405_0H_VS_1.5H_A_PHAGOCYTOPHILUM_STIM_NEUTROPHIL_UP	c7.immunologic.all.GSE2405_0H_VS_1.5H_A_PHAGOCYTOPHILUM_STIM_NEUTROPHIL_UP	Custom	1.09E-05	0.0102
hsa04512	ECM-receptor interaction	KEGG	2.53E-04	0.0108
hsa00620	Pyruvate metabolism	KEGG	2.49E-04	0.0108
c7.immunologic.all.GSE29618_PD_C_VS_MDC_DAY7_FLU_VACCINE_DN	c7.immunologic.all.GSE29618_PD_C_VS_MDC_DAY7_FLU_VACCINE_DN	Custom	1.68E-05	0.0109
c7.immunologic.all.GSE25087_FETAL_VS_ADULT_TREG_DN	c7.immunologic.all.GSE25087_FETAL_VS_ADULT_TREG_DN	Custom	2.01E-05	0.0109
c7.immunologic.all.GSE19198_1H_VS_6H_IL21_TREATED_TCELL_UP	c7.immunologic.all.GSE19198_1H_VS_6H_IL21_TREATED_TCELL_UP	Custom	2.03E-05	0.0109
c7.immunologic.all.GSE16451_CTRL_VS_WEST_EQUINE_ENC_VIRUS_MATURE_NEURON_CELL_LINE_DN	c7.immunologic.all.GSE16451_CTRL_VS_WEST_EQUINE_ENC_VIRUS_MATURE_NEURON_CELL_LINE_DN	Custom	2.24E-05	0.0109
c7.immunologic.all.GSE25123_CTRL_VS_IL4_STIM_MACROPHAGE_UP	c7.immunologic.all.GSE25123_CTRL_VS_IL4_STIM_MACROPHAGE_UP	Custom	2.35E-05	0.0109
c7.immunologic.all.GSE29164_DAY3_VS_DAY7_UNTREATED_MELANOMA_DN	c7.immunologic.all.GSE29164_DAY3_VS_DAY7_UNTREATED_MELANOMA_DN	Custom	3.88E-05	0.0139
c7.immunologic.all.GSE4811_CLASSSSICALY_ACTIVATED_VS_TYPE_2_ACTIVATED_MACROPHAGE_DN	c7.immunologic.all.GSE4811_CLASSSSICALY_ACTIVATED_VS_TYPE_2_ACTIVATED_MACROPHAGE_DN	Custom	4.52E-05	0.0139
c7.immunologic.all.GSE12839_CTRL_VS_IL12_TREATED_PBMC_DN	c7.immunologic.all.GSE12839_CTRL_VS_IL12_TREATED_PBMC_DN	Custom	4.88E-05	0.0139
c6.oncogenic.all.P53_DN.V1_UP	c6.oncogenic.all.P53_DN.V1_UP	Custom	3.52E-05	0.0139
c6.oncogenic.all.RAF_UP.V1_UP	c6.oncogenic.all.RAF_UP.V1_UP	Custom	3.64E-05	0.0139
c4.cgn.MORF_PTPRB	c4.cgn.MORF_PTPRB	Custom	4.34E-05	0.0139
GO:0009119	ribonucleoside metabolic process	GOBP	1.35E-04	0.0155
GO:0016042	lipid catabolic process	GOBP	1.40E-04	0.0158
GO:0071347	cellular response to interleukin-1	GOBP	1.48E-04	0.0165
c7.immunologic.all.GSE2405_0H_VS_9H_A_PHAGOCYTOPHILUM_STIM_NEUTROPHIL_DN	c7.immunologic.all.GSE2405_0H_VS_9H_A_PHAGOCYTOPHILUM_STIM_NEUTROPHIL_DN	Custom	6.61E-05	0.0168
c4.cgn.MORF_TNFRSF6	c4.cgn.MORF_TNFRSF6	Custom	6.59E-05	0.0168
GO:0070647	protein modification by small protein conjugation or removal	GOBP	2.07E-04	0.0202
GO:0072521	purine-containing compound metabolic process	GOBP	2.20E-04	0.0202
GO:0016925	protein sumoylation	GOBP	2.13E-04	0.0202
GO:0044711	single-organism biosynthetic process	GOBP	2.17E-04	0.0202

GO:0006409	tRNA export from nucleus	GOBP	2.36E-04	0.0202
GO:0071431	tRNA-containing ribonucleoprotein complex export from nucleus	GOBP	2.36E-04	0.0202
GO:0001706	endoderm formation	GOBP	2.30E-04	0.0202
GO:0098927	vesicle-mediated transport between endosomal compartments	GOBP	2.43E-04	0.0205
GO:0051031	tRNA transport	GOBP	2.57E-04	0.0209
GO:0045022	early endosome to late endosome transport	GOBP	2.58E-04	0.0209
GO:0043647	inositol phosphate metabolic process	GOBP	2.61E-04	0.0209
GO:0007492	endoderm development	GOBP	2.88E-04	0.0212
GO:0090101	negative regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	GOBP	2.71E-04	0.0212
GO:0071166	ribonucleoprotein complex localization	GOBP	2.80E-04	0.0212
GO:0046434	organophosphate catabolic process	GOBP	2.85E-04	0.0212
c7.immunologic.all.GSE24492_LYVE_NEG_VS_POS_MACROPHAGE_DN	c7.immunologic.all.GSE24492_LYVE_NEG_VS_POS_MACROPHAGE_DN	Custom	8.87E-05	0.0216
GO:0071426	ribonucleoprotein complex export from nucleus	GOBP	3.04E-04	0.0217
GO:0034605	cellular response to heat	GOBP	3.05E-04	0.0217
GO:0016053	organic acid biosynthetic process	GOBP	3.11E-04	0.0218
hsa03320	PPAR signaling pathway	KEGG	7.35E-04	0.0224
GO:0003014	renal system process	GOBP	3.62E-04	0.0244
GO:0006629	lipid metabolic process	GOBP	3.78E-04	0.0249
GO:0072080	nephron tubule development	GOBP	4.17E-04	0.0262
GO:0009126	purine nucleoside monophosphate metabolic process	GOBP	4.15E-04	0.0262
GO:0009167	purine ribonucleoside monophosphate metabolic process	GOBP	4.15E-04	0.0262
GO:0055086	nucleobase-containing small molecule metabolic process	GOBP	4.29E-04	0.0263
c4.cgn.MORF_BRCA1	c4.cgn.MORF_BRCA1	Custom	1.29E-04	0.0274
c4.cgn.MORF_MLLT10	c4.cgn.MORF_MLLT10	Custom	1.32E-04	0.0274
c7.immunologic.all.GSE35543_IN_VITRO_ITREG_VS_CONVERTED_EX_ITREG_UP	c7.immunologic.all.GSE35543_IN_VITRO_ITREG_VS_CONVERTED_EX_ITREG_UP	Custom	1.39E-04	0.0275
c7.immunologic.all.GSE25123_WT_VS_PPARG_KO_MACROPHAGE_ROSIGLITAZONE_STIM_DN	c7.immunologic.all.GSE25123_WT_VS_PPARG_KO_MACROPHAGE_ROSIGLITAZONE_STIM_DN	Custom	1.51E-04	0.0275
c7.immunologic.all.GSE22103_LPS_VS_GMCSF_AND_IFNG_STIM_NEUTROPHIL_UP	c7.immunologic.all.GSE22103_LPS_VS_GMCSF_AND_IFNG_STIM_NEUTROPHIL_UP	Custom	1.52E-04	0.0275
c7.immunologic.all.GSE23984_CTRL_VS_HYPOCALEMIC_VITAMIND_ANALOG_TCELL_UP	c7.immunologic.all.GSE23984_CTRL_VS_HYPOCALEMIC_VITAMIND_ANALOG_TCELL_UP	Custom	1.53E-04	0.0275
c7.immunologic.all.GSE21927_SPLEEN_MONOCYTE_VS_GMCSF_GCSF_BONE_MARROW_DN	c7.immunologic.all.GSE21927_SPLEEN_MONOCYTE_VS_GMCSF_GCSF_BONE_MARROW_DN	Custom	1.63E-04	0.0276
c6.oncogenic.all.ALK_DN.V1_UP	c6.oncogenic.all.ALK_DN.V1_UP	Custom	1.58E-04	0.0276
GO:0060402	calcium ion transport into cytosol	GOBP	4.84E-04	0.0278
GO:0009408	response to heat	GOBP	4.91E-04	0.0280
GO:0070555	response to interleukin-1	GOBP	4.98E-04	0.0281

c7.immunologic.all.GSE13411_SWI TCHED_MEMORY_BCELL_VS_ PLASMA_CELL_DN	c7.immunologic.all.GSE13411_SWITCHED_ME MORY_BCELL_VS_PLASMA_CELL_DN	Custom	1.84E-04	0.0293
c4.cgn.MORF_STK17A	c4.cgn.MORF_STK17A	Custom	1.80E-04	0.0293
GO:0022408	negative regulation of cell-cell adhesion	GOBP	5.46E-04	0.0297
GO:0060401	cytosolic calcium ion transport	GOBP	5.50E-04	0.0297
c7.immunologic.all.GSE30971_CT RL_VS_LPS_STIM_MACROPHA GE_WBP7_KO_2H_DN	c7.immunologic.all.GSE30971_CTRL_VS_LPS_S TIM_MACROPHAGE_WBP7_KO_2H_DN	Custom	1.94E-04	0.0302
GO:0051168	nuclear export	GOBP	5.69E-04	0.0305
GO:0072523	purine-containing compound catabolic process	GOBP	5.82E-04	0.0307
c7.immunologic.all.GSE25123_WT _VS_PPARG_KO_MACROPHAG E_DN	c7.immunologic.all.GSE25123_WT_VS_PPARG_ KO_MACROPHAGE_DN	Custom	2.06E-04	0.0311
c7.immunologic.all.GSE20500_CT RL_VS_RETINOIC_ACID_TREA TED_CD4_TCELL_DN	c7.immunologic.all.GSE20500_CTRL_VS_RETIN OIC_ACID_TREATED_CD4_TCELL_DN	Custom	2.12E-04	0.0312
GO:0045598	regulation of fat cell differentiation	GOBP	6.19E-04	0.0313
GO:2000021	regulation of ion homeostasis	GOBP	6.39E-04	0.0321
GO:0070265	necrotic cell death	GOBP	7.55E-04	0.0344
GO:0030193	regulation of blood coagulation	GOBP	7.79E-04	0.0347
GO:1900046	regulation of hemostasis	GOBP	7.79E-04	0.0347
GO:0006406	mRNA export from nucleus	GOBP	7.93E-04	0.0348
GO:0071427	mRNA-containing ribonucleoprotein complex export from nucleus	GOBP	7.93E-04	0.0348
GO:0009150	purine ribonucleotide metabolic process	GOBP	8.01E-04	0.0350
GO:0032092	positive regulation of protein binding	GOBP	8.28E-04	0.0354
GO:0051186	cofactor metabolic process	GOBP	8.29E-04	0.0354
hallmark.all.HALLMARK_MTOR C1_SIGNALING	hallmark.all.HALLMARK_MTORC1_SIGNALIN G	Custom	2.49E-04	0.0357
c7.immunologic.all.GSE29164_UN TREATED_VS_CD8_TCELL_AN D_IL12_TREATED_MELANOMA _DAY7_DN	c7.immunologic.all.GSE29164_UNTREATED_VS _CD8_TCELL_AND_IL12_TREATED_MELAN OMA_DAY7_DN	Custom	2.62E-04	0.0357
c4.cgn.MORF_MAGEA8	c4.cgn.MORF_MAGEA8	Custom	2.59E-04	0.0357
hallmark.all.HALLMARK_EPITHE LIAL_MESENCHYMAL_TRANSI TION	hallmark.all.HALLMARK_EPITHELIAL_MESE NCHYMAL_TRANSITION	Custom	2.77E-04	0.0369
GO:1900034	regulation of cellular response to heat	GOBP	8.76E-04	0.0371
GO:0006475	internal protein amino acid acetylation	GOBP	8.84E-04	0.0371
GO:0010522	regulation of calcium ion transport into cytosol	GOBP	8.85E-04	0.0371
GO:0030397	membrane disassembly	GOBP	9.48E-04	0.0380
GO:0051081	nuclear envelope disassembly	GOBP	9.48E-04	0.0380
c7.immunologic.all.GSE24142_DN 2_VS_DN3_THYMOCYTE_ADU LT_UP	c7.immunologic.all.GSE24142_DN2_VS_DN3_T HYMOCYTE_ADULT_UP	Custom	3.00E-04	0.0389
c6.oncogenic.all.PTEN_DN.V2_UP	c6.oncogenic.all.PTEN_DN.V2_UP	Custom	3.06E-04	0.0389
GO:0016573	histone acetylation	GOBP	0.00101	0.0399
GO:0019751	polyol metabolic process	GOBP	0.00102	0.0399
GO:0006163	purine nucleotide metabolic process	GOBP	0.00104	0.0403
c7.immunologic.all.GSE25087_TR EG_VS_TCONV_FETUS_UP	c7.immunologic.all.GSE25087_TREG_VS_TCON V_FETUS_UP	Custom	3.34E-04	0.0415
GO:0050818	regulation of coagulation	GOBP	0.0011	0.0417

c7.immunologic.all.GSE35543_IN_VIVO_NTREG_VS_CONVERTED_EX_ITREG_DN	c7.immunologic.all.GSE35543_IN_VIVO_NTREG_VS_CONVERTED_EX_ITREG_DN	Custom	3.81E-04	0.0444
GO:0021953	central nervous system neuron differentiation	GOBP	0.00127	0.0474
c7.immunologic.all.GSE12366_PLASMA_CELL_VS_NAIVE_BCELL_UP	c7.immunologic.all.GSE12366_PLASMA_CELL_VS_NAIVE_BCELL_UP	Custom	4.37E-04	0.0481
c7.immunologic.all.GSE26488_WT_VS_VP16_TRANSGENIC_HDAC7_KO_DOUBLE_POSITIVE_THYMOCYTE_DN	c7.immunologic.all.GSE26488_WT_VS_VP16_TRANSGENIC_HDAC7_KO_DOUBLE_POSITIVE_THYMOCYTE_DN	Custom	4.38E-04	0.0481
GO:0007077	mitotic nuclear envelope disassembly	GOBP	0.0013	0.0482
c7.immunologic.all.GSE6674_UNSTIM_VS_PL2_3_STIM_BCELL_UP	c7.immunologic.all.GSE6674_UNSTIM_VS_PL2_3_STIM_BCELL_UP	Custom	4.53E-04	0.0485
c6.oncogenic.all.CAHOY_ASTROGLIAL	c6.oncogenic.all.CAHOY_ASTROGLIAL	Custom	4.60E-04	0.0485
GO:0006913	nucleocytoplasmic transport	GOBP	0.00133	0.0490
GO:0045444	fat cell differentiation	GOBP	0.00135	0.0491
GO:0018393	internal peptidyl-lysine acetylation	GOBP	0.00136	0.0491
c7.immunologic.all.GSE17721_CTRL_VS_PAM3CSK4_8H_BMDC_UP	c7.immunologic.all.GSE17721_CTRL_VS_PAM3CSK4_8H_BMDC_UP	Custom	4.75E-04	0.0492
GO:0072009	nephron epithelium development	GOBP	0.00138	0.0495
c4.cgn.MORF_BCL2	c4.cgn.MORF_BCL2	Custom	4.87E-04	0.0495

Table S4. Real time PCR primers for human gene expression studies.

Gene symbol	Forward primer	Reverse primer
<i>ASH1L</i>	CCAGGAAGGGCTGTGTTGAT	CTGGTTACAGCATTGCTCGC
<i>PGK1</i>	AAGGGAAGCGGGTCGTTATG	TGGGACAGCAGCCTTAATCC
<i>CCAT1</i>	AAGCAGGCAGAAAGCCGTAT	TCAAATGGCCATCCACACCT
<i>B2M</i>	TAAGTGGGATCGAGACATGTAAGC	AATCCAAATGCGGCATCTTCAA
<i>SLC6A15</i>	GCCTTGGGATCAGTGTCTT	AGGTGGTGGCAGAACTTTGT
<i>NNMT</i>	GCACTCTGCAGAAAGCCAGA	CAGCAGGTCTCCCTTCACAC
<i>TSSC2</i>	GCAGGAGCAGAACCCGAAT	CAGCTCGCTCTGCACTGTTT
<i>ONECUT3</i>	GGATCCTGTGTCGCTCTCAG	GATTTGAGCTTGCTCCACGG
<i>HAPLN1</i>	CTGTTGTGGTAGCACTGGACT	GCCCCAGTCGTGGAAAGTAA
<i>LINC01929</i>	GAACCATGGGTTGGCTCTGA	TATGGGCTCCGGGAAAACAC
<i>LINC00173</i>	CCAGAATCGGGGTGGATCAG	CCTGCAGCACGCAATTAGAC
<i>IL6</i>	CCAGAGCTGTGCAGATGAGT	ATTTGTGGTTGGGTCAGGGG
<i>PRDM9</i>	GCATCAAGTGGGGCAGCA	AAAGGCCAGACAGCATGAGG