Supplemental Table 1. Expression data of 547 transcripts consistently deregulated in *Hdac1* $^{\Delta/\Delta}$;*Hdac2*$^{\Delta/+}$ pre-leukemic thymocytes and tumors. Indicated are fold changes (FC) values in RNA levels of indicated transcripts in *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{\Delta/+}$ lymphomas compared to wild type thymocytes.

Supplemental Table 2. Common Targeted Genes(CTGs) (De Jong et al. 2011) that show deregulated expression in *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{\Delta/+}$ pre-leukemic thymocytes and tumors. CTGs are ranked according to the number of times (counts) that a gene was targeted by a retroviral insertion (De Jong et al. 2011).

Supplemental Table 3. Gene ID of transcripts commonly deregulated in *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$, *Hdac1*$^{\Delta/\Delta}$ and *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ lymphomas.

Supplementary Table 1. Deregulated transcripts in 1 and 3 week old *Hdac1Δ/Δ;Hdac2Δ/+* thymocytes and *Hdac1Δ/Δ;Hdac2Δ/+* lymphoma

Symbol	RefSeq_ID	logFC wt vs lymphoma	adj.P.Val
Gm525	NM_001033266.2	96.54925253	2.84E-06
Ddc		44.04000132	6.42E-08
Ddc	NM_016672.3	35.93240336	2.65E-08
Gm525	NM_001033266.2	33.14844652	3.55E-09
Stra8	NM_009292.1	5.015000451	0.018457156
Cacng4	NM_019431.1	4.837170227	0.000612326
Sh3gl3	NM_017400.2	4.575282778	5.94E-07
Rbfox3	NM_001039167.1	4.476790573	4.04E-05
Rbfox3	NM_001039168.1	4.244831479	3.59E-05
Slc6a13	NM_144512.2	4.187409776	1.13E-05
Epb4.1l5	NM_145506.2	3.993392169	0.001620121
Cd276	NM_133983.3	3.956035374	1.49E-05
Jdp2	NM_030887.2	3.841963852	3.18E-06
Prelid2	NM_029942.1	3.593340396	0.025890601
Tro	NM_001002272.2	3.580300991	0.019614954
Epb4.1l5	NM_145506.3	3.567420852	0.001123159
Lpar2	NM_020028.3	3.487778085	0.000173714
5730559C18Rik		3.381768451	0.040133817
Tro	NM_001002272.2	3.374714572	0.017570953
Mfap2	NM_008546.2	3.365703042	0.028247993
Wdr86	NM_026621.1	3.293029345	0.000525288
Tro	NM_001002272.2	3.250569704	0.040618715
1110008L16F	XM_126928.4	3.239076787	0.000136508
Sdc1	NM_011519.2	3.186263712	1.81E-05
Aif1l	NM_145144.1	3.128563074	6.97E-07
Ldhd	NM_027570.3	3.126732053	0.001355712
Ephb2	XM_204072.3	3.120573348	5.62E-06
Jazf1	NM_173406.2	3.029323518	4.64E-05
Kcnab3	NM_010599.3	3.02889007	7.56E-05
Pdgfrb	NM_008809.1	3.025051746	0.000273137
Sdc1	NM_011519.1	3.008436367	9.00E-06
Rnd2	NM_009708.1	2.904524471	0.005919195
Sema6b	XM_001004114.1	2.889667714	0.00379049
Scn5a	NM_021544.3	2.880488903	0.000797838
Syne2	NM_001005510.2	2.832655556	2.67E-05
Sema4g	NM_011976.1	2.791069962	2.32E-06
Bsn	NM_007567.2	2.785697634	0.000931492
Sox12	NM_011438.2	2.757922017	0.002579387
2010107G12Rik		2.757461129	0.000807757
H1f0	NM_008197.3	2.742652625	1.81E-05
Dorz1		2.671412717	0.000199131

Zfhx3	NM_007496.2	2.670418623	0.006137236
Zfp365	NM_178679.2	2.642504966	0.001128143
Ttc26	NM_153600.2	2.631064217	0.000322905
Abhd14a	NM_145919.1	2.612391507	0.00129276
Gmnn	NM_020567.1	2.568298549	7.89E-05
Rem2	NM_080726.3	2.510600358	0.002169129
Wnt8b	NM_011720.2	2.486619906	5.65E-05
Serp2	XM_894566.3	2.484530087	0.048775535
2010107G12	NM_001025573.1	2.452045735	0.00118972
Slc29a1		2.412191669	1.12E-05
Kctd17	NM_001081367.1	2.389305761	6.54E-05
Ramp3	NM_019511.1	2.370558963	0.006288021
Wnt5b	NM_009525.2	2.367642872	0.002886903
Nphp4	NM_153424.2	2.340201501	1.24E-07
Spef1	NM_027641.2	2.334575349	0.000210506
Sox12	NM_011438.2	2.311943899	0.002360491
8430427H17	NM_001001986.1	2.309885312	0.0001176
Cnnm1	NM_031396.1	2.302843749	0.023079399
7-Sep	NM_033144.1	2.292335197	0.000278585
Ramp3	NM_019511.1	2.280405944	0.026136053
Reep1	NM_178608.2	2.265024978	0.00643244
Wdr67	NM_001081396.1	2.261887018	1.16E-05
Lama5	NM_001081171.2	2.261605929	0.004856707
Hlcs	NM_139145.4	2.259034415	0.000263798
Mcoln2	NM_001005846.2	2.248318002	0.000299633
Rilpl1	NM_021430.2	2.247543908	0.000546043
C430017H16	XM_143616.3	2.246474677	0.000357029
Pvrl2	NM_008990.2	2.244663413	0.001524703
Ramp3	NM_019511.3	2.24056284	0.019791614
Zfp704	NM_133218.1	2.23420481	0.020828312
Fgd1	NM_008001.3	2.208909875	0.002944722
Prickle1	NM_001033217.3	2.198491872	0.000106679
Zfp365	XM_980150.1	2.193803383	0.001572303
3230401I01Rik		2.18538419	0.002284046
Lpar2	NM_020028.3	2.158594953	0.019116488
E130012A19	NM_175332.3	2.136957441	0.000639578
LOC674960	XR_004709.2	2.132483908	9.30E-05
Slc12a8	NM_001083902.1	2.1267519	0.003594056
Klhl5		2.123044699	0.000208482
D130067N01Rik		2.117154502	0.000650056
Nln	NM_029447.2	2.116564724	0.000524798
Ldhd	NM_027570.3	2.108700229	0.012432456
1810007P19	NM_172701.2	2.105433403	0.000439039
Fgfr1	NM_010206.2	2.088391068	0.011758274
9430038I01R	XM_917763.2	2.076818188	3.10E-05
Gm347	NM_001005420.1	2.062334539	0.000238691

Slc22a21	NM_019723.2	2.056403511	0.0121836
Syde1	XM_359260.3	2.043483433	0.001609289
Dyrk3	NM_145508.2	2.020562536	0.000198301
Ldhd	NM_027570.3	2.013775721	0.018559588
Rsph1	NM_025290.3	2.010742564	0.005807852
Klhl5		1.988936966	0.000165706
Dnalc1	NM_028821.2	1.988730784	0.004822477
Spats1	NM_027649.2	1.97995278	0.001151247
E430003D02Rik		1.967460842	0.001226778
Garnl3	NM_178888.4	1.955920037	0.000268465
Wdr31	NM_023597.1	1.944345899	0.01013547
Pmm1		1.943658177	0.002188367
A830048E23Rik		1.93935147	0.015080712
Zfhx3	NM_007496.2	1.933174126	0.045283369
Arvcf		1.925687699	0.007750254
Mcam	NM_023061.1	1.918362687	0.002705271
1110036O03	NM_176830.2	1.901867504	0.0157994
Zfp599	NM_181419.2	1.875587591	0.00434829
Shq1	NM_181590.3	1.87230707	0.000159888
Nt5dc2	NM_027289.1	1.855082529	2.67E-06
Pvrl2	NM_008990.2	1.854434159	0.009870619
E330016A19	NM_173386.3	1.849911661	3.12E-05
Bag2	NM_145392.2	1.849394852	0.000676459
Prpf40b	NM_018786.1	1.847713109	9.07E-05
Arsi	NM_001038499.1	1.841782518	0.0244838
9430038I01R	XM_925223.2	1.838653776	1.37E-05
D030034I04Rik		1.836812761	1.33E-05
Armc9	NM_027456.1	1.836471206	0.002476749
Prpf40b	NM_018786.2	1.821367327	7.72E-05
Thg1l	NM_001080969.1	1.790908767	0.000397305
Pcbp4	NM_021567.2	1.781167326	0.000355625
Spag4	NM_139151.4	1.752102653	0.00232422
Mcam	NM_023061.1	1.744227085	0.000454923
Lpcat4	NM_207206.1	1.72415551	0.002452552
Cox6b2	NM_183405.1	1.718817326	0.003359413
Rwdd2		1.717692448	9.57E-05
Rcl1	NM_021525.2	1.70283173	0.000512117
Nlgn2	NM_198862.2	1.685722235	0.000398157
Zfp41	NM_011759.1	1.64096609	1.71E-05
Nln	NM_029447.1	1.633764522	9.62E-05
Igf2bp2	NM_183029.1	1.629075934	0.005546777
Stab1	NM_138672.2	1.619899995	3.18E-06
2700050C19Rik		1.616080041	0.018693572
Purg	NM_001098233.1	1.61334545	0.014277099
Rilpl1	NM_021430.2	1.609586206	0.000247644
1700010H15Rik		1.606109189	0.005594331

Dclk2	NM_027539.3	1.602772698	0.049210011
Kctd17	NM_001081367.1	1.599954295	0.00065556
Fbxw8	NM_172721.2	1.599930284	9.69E-05
Nln	NM_029447.1	1.593474326	0.000184561
5330431N19	NM_172639.1	1.583225311	1.30E-05
Ccdc109a	NM_001033259.2	1.582794325	0.008486695
D130074M14Rik		1.575716363	0.000351517
BC066107	NM_207245.1	1.569333418	0.005919195
Pkig	NM_001039391.1	1.561817479	0.000475517
Xrcc6	NM_010247.2	1.558804449	0.00250503
Pbx3	NM_016768.1	1.552821481	0.006443228
Itpka	NM_146125.1	1.550150727	0.004609261
Isyna1	NM_023627.1	1.549821962	0.000996137
Dis3	NM_028315.2	1.547959642	0.000279773
Fbxo44	NM_173401.2	1.540969786	6.46E-05
4833427B12Rik		1.532322346	0.000274425
Pmm1	NM_013872.2	1.531330604	0.000229923
Espl1	NM_001014976.1	1.521870218	3.51E-05
2610301B20	NM_026005.2	1.520836109	3.18E-05
Grwd1	NM_153419.1	1.484102383	0.000263815
Impa2		1.469402591	4.51E-05
Gins2	NM_178856.1	1.465245662	6.88E-05
Zfp365	XM_980076.1	1.461924199	0.03401545
Tpi1	NM_009415.1	1.459581583	6.70E-05
5330431N19	NM_172639.1	1.455136655	0.000199131
Tmem201	NM_001025106.1	1.452909031	0.001276681
3830430K15Rik		1.446205755	5.34E-05
LOC1000483	XM_001480281.1	1.434673287	0.000909188
Tex9	NM_009359.2	1.425094305	0.000668896
Apex1	NM_009687.1	1.415178458	0.003955312
Pmm1	NM_013872.1	1.41300665	4.82E-05
Slc7a7	NM_011405.3	1.412204342	0.004150882
Morn2	NM_194269.1	1.404458839	9.05E-05
Wwc2	NM_133791.4	1.40441557	0.000916446
D15Ertd682e	NM_028003.1	1.404171361	9.63E-06
Slc29a1	NM_022880.1	1.396000221	0.000664102
Prr13	NM_025385.2	1.382210323	0.001476747
AU022508		1.378787657	0.000849123
LOC677144	XM_001004138.1	1.378763701	5.34E-05
Dcun1d4	NM_178896.4	1.37558953	0.000709678
Elf2	NM_023502.1	1.374903777	0.005853236
LOC1000483	XR_034455.1	1.371083771	0.002142924
3110013H01	XM_203393.1	1.370732536	0.020724235
Yaf2	NM_024189.5	1.361760866	0.000175354
Myc	NM_010849.4	1.361751485	0.016803067
Llph	NM_025431.2	1.34342549	0.001108178

Wdr31	NM_023597.1	1.338131346	0.013441711
4833426H15Rik		1.330589204	0.033442054
Tpi1	NM_009415.1	1.328240597	7.94E-05
1500009L16F	XM_899407.2	1.324485733	0.030877604
Ctnnbip1	NM_023465.3	1.317058448	0.014767001
Renbp	NM_023132.2	1.316864188	0.000488088
Xrcc6	NM_010247.2	1.31605386	0.032686667
BC022687	NM_145450.3	1.310744998	0.033928052
Med22	NM_001033908.1	1.298405115	0.000192943
Faf1	NM_007983.2	1.279518365	2.94E-05
Usp2	NM_198091.2	1.26963347	0.003683843
Stk3	NM_019635.2	1.269292591	0.012247074
Ipo5	NM_023579.4	1.258136771	0.000774228
R74862	NM_133790.1	1.258019524	0.035015617
3010003L21F	XR_005252.1	1.254988335	0.025791325
Dut	NM_023595.5	1.252346486	0.000510219
2010317E24I	XM_130053.2	1.247580674	0.000943192
Unc119	NM_011676.2	1.246826387	0.032529429
Zfp446	NM_175558.2	1.23707994	0.000260089
scl000408.1_	AK009508.1	1.228599949	0.000846402
Stk3		1.222551834	0.005499363
Stard6	NM_029019.3	1.213146257	0.001385926
Nup37	NM_028334.3	1.212825019	0.004583377
Tspan6	NM_019656.3	1.209496793	0.040030082
BC039210	XM_001481316.1	1.208644409	0.000114783
4930570C03I	NM_026353.2	1.207995744	0.000139549
Zfp446	NM_175558.3	1.20436533	0.000335742
Slc7a7	NM_011405.1	1.200592906	0.00715605
Cask	NM_009806.2	1.194973686	0.043183428
LOC384338	XM_357585.1	1.194484847	0.00153554
LOC1000476	XM_001478602.1	1.189443822	0.000828019
Gale	NM_178389.3	1.176783092	0.003150163
Zkscan17	NM_172941.2	1.163170105	0.000135789
Gale	NM_178389.3	1.161748227	0.00706131
Gins2	NM_178856.1	1.139643216	0.000178525
Phf13	NM_172705.1	1.137612529	0.00233663
Tmem107	NM_025838.1	1.135852532	0.001294375
Trip10	NM_134125.3	1.122147791	0.00335773
Shmt1		1.115740034	0.049448477
Polr2f	NM_027231.1	1.111316007	8.96E-05
Grwd1	NM_153419.1	1.104800228	0.00645402
Prdx4	NM_016764.3	1.090759625	7.74E-05
Larp2	NM_001040399.1	1.087268296	0.047695765
1110031I02R	NM_025402.1	1.084653989	6.94E-05
A130027D22Rik		1.079216666	0.038703279
Cercam	NM_207298.2	1.070269131	0.015660678

Tmem201	NM_001025106.1	1.056129969	0.007272285
A830080H07Rik		1.054811817	0.001098973
Acpl2	NM_153420.2	1.045773123	0.001172405
Wdr77	NM_027432.3	1.036586132	0.000361599
1810055G02	NM_028077.2	1.020850234	0.005492999
scl0004175.1	BC026739.1	1.004724937	0.00342796
Plcb3	NM_008874.2	0.99773697	0.01263227
Tens1		0.984025592	0.012817824
Pus1	NM_001025561.2	0.981654366	0.033466387
EG667190	XR_002058.1	0.973065228	0.000875419
Rcl1	NM_021525.2	0.971016335	0.01543775
Tens1		0.969135879	0.014000496
Nutf2	NM_026532.3	0.968814462	0.003330524
Ahsa2	NM_172391.3	0.966724754	0.002142924
Elovl1	NM_001039175.1	0.94518611	0.001485345
5330431N19	NM_172639.2	0.934093619	0.000911211
Arrb1	NM_178220.3	0.931656168	0.046363015
Asb1	NM_023046.4	0.929433721	0.007356093
2410015N17	NM_023203.1	0.927121563	0.004899855
Dph3	NM_001047433.1	0.913814003	0.005422149
Pabpc4	NM_148917.2	0.911388822	0.022522421
Rcl1	NM_021525.2	0.905947026	0.014735553
BC022224	NM_177564.4	0.905060387	0.022719683
Azi1	NM_009734.1	0.900801726	0.00697379
LOC383897	XM_357315.1	0.895363975	0.040030082
Gpsm1	NM_153410.2	0.891828448	0.001921997
Hexdc	NM_001001333.1	0.883360088	0.001189752
Mycbp	NM_019660.3	0.84784789	0.008795821
Palm	NM_023128.2	0.844174007	0.004569138
Limk1	NM_010717.2	0.832017102	0.009702118
Edg5		0.795125996	0.043358676
Sntb2		0.794964652	0.007473387
Ssx2ip	NM_138744.2	0.791576683	0.009718781
Adk	NM_134079.3	0.790942802	0.008070294
Kif3a	NM_008443.3	0.778974601	0.021041703
Mycbp	NM_019660.2	0.764821416	0.008811184
Gpsm1	NM_153410.4	0.720499866	0.00842765
Phlpp	XM_900133.2	0.716723055	0.024576864
D15Mit260		0.714906251	0.003243574
Nudt22	NM_026675.2	0.675306805	0.047256714
ENSMUSG00	NM_145433.1	0.648205709	0.017980137
1810027O10	XM_109683.4	0.616920537	0.013402026
Pes1	NM_022889.3	0.591457499	0.029061048
Rnf170	NM_029965.2	-0.614763648	0.035433303
Pik3cg		-0.775255843	0.032921845
Psd4	NM_177611.3	-0.806842619	0.001553505

Lime1	NM_023684.2	-0.892603415	0.032521409
Traf2	NM_009422.2	-0.89372469	0.03359778
Plxnd1	NM_026376.3	-0.895475023	0.006410485
Sla2	NM_029983.4	-0.901195488	0.028932613
6230425C21Rik		-0.963435917	0.00667561
Epc1	NM_007935.1	-0.99906246	0.000573522
Sit1	NM_019436.1	-1.014132418	0.021397792
Scarb2	NM_007644.2	-1.022889427	0.001924468
Mgea5		-1.025379416	0.007126769
Birc2	NM_007465.1	-1.060411821	2.39E-05
Hmha1	NM_027521.2	-1.061963798	0.002551125
AA960436	NM_133954.1	-1.078321213	0.020261384
Rnf167	NM_027445.1	-1.10536411	0.00079799
Clk3	NM_007713.3	-1.10570276	0.001030088
Map4k2	NM_009006.2	-1.113315841	0.00161144
9530018I07Rik		-1.122250591	0.018235705
Epc1	NM_007935.1	-1.127655398	0.000586672
Rasl11b	NM_026878.1	-1.136024161	0.038991515
5430411K18I	XM_916282.3	-1.136026376	0.00018389
Rasl11b	NM_026878.1	-1.139589715	0.038209582
Prrt1	NM_030890.1	-1.14964284	0.041942767
Trim56	NM_201373.3	-1.154817813	0.003524534
Parp6	NM_029922.2	-1.170409881	0.003517831
Snx15	NM_026912.1	-1.191356542	0.000379479
Rnf167	NM_027445.1	-1.19276231	0.00031193
Snapc3	NM_029949.1	-1.20325568	0.000710524
6330442E10I	NM_178745.3	-1.20535179	0.02232689
Itk	NM_010583.2	-1.209197393	0.004741862
LOC1000483	XM_001479795.1	-1.214979127	0.002752797
Znrf1	NM_133206.2	-1.220667819	0.000146699
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Il2rg		-1.23414166	0.00098419
Apoa4	NM_007468.2	-1.238869587	0.032629774
Tmem77	NM_026013.2	-1.240744658	0.000911211
Klf7		-1.245431748	0.001751613
Nfatc3		-1.249101449	0.010224774
Rcan3	NM_022980.4	-1.263661892	0.001548296
Nfkbid	NM_172142.3	-1.263966483	0.003871882
Dscr1l2	NM_022980.3	-1.270305451	0.001836703
Rnf167	NM_027445.1	-1.285018459	0.00096234
5830432E09I	XM_150021.1	-1.29585684	0.035015617
LOC380617	XM_149644.3	-1.297724254	0.005358954
AI987692	NM_177912.2	-1.308393848	0.033555985
Ppfibp2	NM_008905.1	-1.335976395	0.030319625
Pdlim2	NM_145978.1	-1.339664659	0.035280502
Mllt11	NM_019914.3	-1.348140697	0.000142676

0610010K14	NM_026757.1	-1.351417359	0.003987764
Vim	NM_011701.3	-1.381902494	0.001080488
A430106G13Rik		-1.382622494	0.044287367
Ogt	NM_139144.2	-1.389461051	0.000345944
Msn		-1.394748233	6.54E-05
2410019G02	XM_126427.5	-1.39703531	0.001479165
Chchd2	NM_024166.4	-1.411311858	0.000260089
Ogt	NM_139144.2	-1.412198795	0.000188421
Ppp1r3b	NM_177741.3	-1.415432647	0.003740258
Lcp2		-1.436919256	0.005492429
A130010J15F	NM_181048.2	-1.443491979	0.000753524
A930024E05	XR_005345.1	-1.457036255	0.013065294
Arhgap4	NM_138630.1	-1.457068794	0.000157739
Inpp5d	NM_010566.1	-1.467515894	0.005745807
Nedd9	NM_017464.2	-1.472157182	0.002113372
Sdcbp2	NM_145535.1	-1.475832563	0.0052739
Arhgef6	NM_152801.1	-1.477004142	0.013726151
Rgs14	NM_016758.2	-1.478688954	0.000821696
Il28ra	NM_174851.2	-1.489332651	0.011448565
Nedd9	NM_017464.2	-1.496788222	0.004856707
Znf512b	XM_977462.2	-1.504268021	0.015484765
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Tmub1	NM_022418.1	-1.5320419	0.000340387
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Itk		-1.586174519	0.008247325
9030607L17F	NM_027829.1	-1.587539984	0.006154936
2010007L08Rik		-1.588215834	0.031819323
Foxp3	NM_054039.1	-1.591744097	0.006050222
Abi3		-1.600222745	0.049040934
LOC1000473	XM_001477963.1	-1.60109297	0.000728273
LOC545238	NM_001034897.1	-1.626727386	0.018008996
Aim1	NM_172393.1	-1.627395367	0.019794029
Dock10	XM_129913.4	-1.630793564	0.046170573
Il23a	NM_031252.2	-1.636443327	0.023704956
Btg1	NM_007569.1	-1.639232349	0.000128302
Cd84	NM_013489.1	-1.640690325	2.02E-05
Atg10	NM_025770.3	-1.643765197	0.000208536
Ap3m2	NM_029505.1	-1.660985046	0.004661298
Vamp1	NM_009496.2	-1.687877827	0.002341554
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Ypel3	NM_025347.1	-1.695634977	0.000568145
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Vamp1	NM_001080557.1	-1.723465836	0.001670058

Btla	NM_177584.3	-1.731381783	0.03448067
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Gm889	NM_001033437.1	-1.745629796	0.024600014
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LOC226017	XM_129164.2	-1.803024036	0.011076116
A430031F07Rik		-1.817605492	0.018771435
Obfc2a	NM_028696.2	-1.818436547	9.57E-05
Gtdc1	NM_172662.1	-1.819958816	0.00036389
Ankrd6	NM_080471.3	-1.832945745	0.046672081
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LOC332579	XM_285326.2	-1.930812689	0.01498736
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LOC383153	XM_356899.1	-1.958951883	0.007083297
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Ebi3	NM_015766.2	-2.049399767	0.002106202
Fbxw17	NM_175401.3	-2.051995855	0.004822477
Nptx2	NM_016789.2	-2.061879093	0.00727257
B3gnt8	NM_146184.4	-2.075380529	0.000650056
Bcl2a1b	NM_007534.1	-2.079431627	0.006112507
Krt84	NM_008474.1	-2.097742435	0.000263798
LOC623121	XM_001480713.1	-2.109298806	9.30E-05
Inpp4b	NM_001024617.2	-2.122152124	0.004580873
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Dhx58	NM_030150.2	-2.134954389	0.000355625
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LOC380706	XM_354621.1	-2.159096213	0.004601405
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Creld1	NM_133930.1	-2.172131478	6.46E-05
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Muc1	NM_013605.1	-2.247515476	0.00645402
Ncf1	NM_010876.2	-2.262417411	0.005852525
Klk1b9	NM_010116.1	-2.272405538	0.000134676
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Camkk1	NM_018883.2	-2.288971133	0.013988482
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Ankrd6	NM_080471.3	-2.338491405	0.001792436
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Dgka	NM_016811.2	-2.362821594	0.004571092
Dhrs3	NM_011303.4	-2.370197107	2.73E-06
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Gpr146	NM_001038703.1	-2.389340585	0.005672507
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Phxr4	NM_008835.1	-2.426234986	0.000709657
Samhd1	NM_018851.2	-2.426565876	0.00109112
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Samd9l	XM_620286.3	-2.533188659	0.001760796
Centd1	XM_001001363.1	-2.534260552	0.000192943
Hcst	NM_011827.2	-2.544725767	0.002446316
Gpr174	NM_001033251.2	-2.54475138	0.001931412
Gbp2	NM_010260.1	-2.558750734	0.003379243
Ankrd50	NM_001033198.2	-2.573296682	0.000115689
Cd4	NM_013488.2	-2.593869206	0.025284191
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Cdx1	NM_009880.2	-2.652678635	0.000178525
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Hsd11b1	NM_008288.1	-2.708690022	0.006353535

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Gimap1	NM_008376.3	-2.738213702	0.031929166
Lypd6b	NM_027990.3	-2.748245071	0.006739663
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Prodh	NM_011172.1	-3.046801469	0.000649701
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Irf6	NM_016851.2	-3.097065288	0.012759773
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Tctex1d1	NM_026100.2	-3.744178342	0.011836577
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Il4i1	NM_010215.2	-3.811988962	0.001865193
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Rag2	NM_009020.3	-4.962174348	1.55E-06
Tctex1d1	NM_026100.2	-5.090313485	9.78E-07
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Krtdap	NM_001033131.1	-5.705423794	4.03E-09
Cd69	NM_001033122.3	-6.083953428	0.000864261
LOC665446	XM_977005.1	-7.99169934	1.20E-06

Supplementary Table 2. Commonly deregulated transcripts in *Hdac1+/Δ;Hdac2Δ/Δ*, *Hdac1Δ/Δ* and *Hdac1Δ/Δ;Hdac2Δ/+* lymphomas

Gene ID
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ZKSCAN17
ZNRF1

Supplementary Table 3. Common Targeted Genes (CTGs) deregulated in *Hdac1Δ/Δ;Hdac2Δ/+* thymocytes and lymphoma

Gene symbol	Rank	Count	Ensembl ID
MYC	2	340	ENSMUSG00000022346
JDP2	14	81	ENSMUSG00000034271
CCND2	27	35	ENSMUSG00000000184
CD52	46	21	ENSMUSG00000000682
1190002H23RIK	49	21	ENSMUSG00000022018
MGAT4A	114	14	ENSMUSG00000026110
JAZF1	130	13	ENSMUSG00000063568
2010107G12RIK	206	10	ENSMUSG00000029847
STK3	307	8	ENSMUSG00000022329
XRCC6	309	8	ENSMUSG00000022471
SLA2	326	8	ENSMUSG00000027636
CD69	336	8	ENSMUSG00000030156
LDHD	341	8	ENSMUSG00000031958
ARRB1	395	7	ENSMUSG00000018909
NEDD9	404	7	ENSMUSG00000021365
ETNK1	448	7	ENSMUSG00000030275
FGFR1	457	7	ENSMUSG00000031565
LCP2	508	6	ENSMUSG00000002699
ISYNA1	531	6	ENSMUSG00000019139
PDLIM2	548	6	ENSMUSG00000022090
RPAP3	553	6	ENSMUSG00000022466
GTDC1	628	6	ENSMUSG00000036890
TXNIP	631	6	ENSMUSG00000038393
ARMC9	648	6	ENSMUSG00000062590
KIF3A	706	5	ENSMUSG00000018395
CDK20	729	5	ENSMUSG00000021483
CD96	745	5	ENSMUSG00000022657
DCLK2	798	5	ENSMUSG00000028078
GALE	803	5	ENSMUSG00000028671
CASK	829	5	ENSMUSG00000031012
AP3M2	833	5	ENSMUSG00000031539
GINS2	836	5	ENSMUSG00000031821
USP2	839	5	ENSMUSG00000032010
FAM65B	859	5	ENSMUSG00000036006
PRODH	951	4	ENSMUSG00000003526
TNS3	1017	4	ENSMUSG00000020422
TMEM107	1028	4	ENSMUSG00000020895
1110008L16RIK	1032	4	ENSMUSG00000021023
BIN1	1082	4	ENSMUSG00000024381
RBFOX3	1100	4	ENSMUSG00000025576
SAMHD1	1149	4	ENSMUSG00000027639

WDR31	1161	4	ENSMUSG00000028391
PLXND1	1187	4	ENSMUSG00000030123
AQP9	1216	4	ENSMUSG00000032204
BSN	1224	4	ENSMUSG00000032589
PKIG	1245	4	ENSMUSG00000035268
WNT8B	1251	4	ENSMUSG00000036961
INPP4B	1253	4	ENSMUSG00000037940
ACPL2	1278	4	ENSMUSG00000043587
8430427H17RIK	1308	4	ENSMUSG00000061411
ARVCF	1337	3	ENSMUSG00000000325
ZNF512B	1342	3	ENSMUSG00000000823
SPO11	1385	3	ENSMUSG00000005883
STX1A	1402	3	ENSMUSG00000007207
FAF1	1413	3	ENSMUSG00000010517
PABPC4	1414	3	ENSMUSG00000011257
DYRK3	1433	3	ENSMUSG00000016526
DHX58	1442	3	ENSMUSG00000017830
MRM1	1445	3	ENSMUSG00000018405
ITK	1465	3	ENSMUSG00000020395
ZKSCAN17	1467	3	ENSMUSG00000020472
ATG10	1495	3	ENSMUSG00000021619
WDR67	1508	3	ENSMUSG00000022364
SLC38A1	1528	3	ENSMUSG00000023169
KLF7	1589	3	ENSMUSG00000025959
ICOS	1590	3	ENSMUSG00000026009
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CTNNBIP1	1654	3	ENSMUSG00000028988
TEC	1663	3	ENSMUSG00000029217
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ISG15	1745	3	ENSMUSG00000035692
ZFHX3	1769	3	ENSMUSG00000038872
F13A1	1772	3	ENSMUSG00000039109
EDARADD	1773	3	ENSMUSG00000039309
5430411K18RIK	1784	3	ENSMUSG00000039840
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GMNN	2038	2	ENSMUSG00000006715
NUTF2	2053	2	ENSMUSG00000008450
MCOLN2	2070	2	ENSMUSG00000011008
ABI3	2116	2	ENSMUSG00000018381
KCNAB3	2118	2	ENSMUSG00000018470
NLN	2232	2	ENSMUSG00000021710
PARP8	2234	2	ENSMUSG00000021725

BCL6	2269	2	ENSMUSG00000022508
YAF2	2275	2	ENSMUSG00000022634
SLC29A1	2303	2	ENSMUSG00000023942
RSPH1	2305	2	ENSMUSG00000024033
LYPD6B	2437	2	ENSMUSG00000026765
GPSM1	2447	2	ENSMUSG00000026930
DUT	2456	2	ENSMUSG00000027203
DRAM2	2489	2	ENSMUSG00000027900
EPHB2	2529	2	ENSMUSG00000028664
SCARB2	2578	2	ENSMUSG00000029426
STRA8	2596	2	ENSMUSG00000029848
TRAT1	2624	2	ENSMUSG00000030775
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TEX9	2682	2	ENSMUSG00000032219
LACTB	2687	2	ENSMUSG00000032370
SYDE1	2711	2	ENSMUSG00000032714
CDC42EP3	2756	2	ENSMUSG00000036533
SYDE2	2758	2	ENSMUSG00000036863
ARAP2	2785	2	ENSMUSG00000037999
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ANKRD6	2824	2	ENSMUSG00000040183
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5730559C18RIK	2846	2	ENSMUSG00000041605
ZFPM1	2897	2	ENSMUSG00000049577
SERPINB12	2948	2	ENSMUSG00000059956
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DENND1C	3125	1	ENSMUSG00000002668
RELB	3136	1	ENSMUSG00000002983
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ELOVL1	3228	1	ENSMUSG00000006390
CCDC109A	3281	1	ENSMUSG00000009647
LAMA5	3339	1	ENSMUSG00000015647
NCF1	3354	1	ENSMUSG00000015950
HSD11B1	3357	1	ENSMUSG00000016194
CENPV	3388	1	ENSMUSG00000018509
DDC	3452	1	ENSMUSG00000020182
CAMKK1	3501	1	ENSMUSG00000020785
SMOC1	3532	1	ENSMUSG00000021136
EPC1	3792	1	ENSMUSG00000024240
CDX1	3833	1	ENSMUSG00000024619
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PARP6	3894	1	ENSMUSG00000025237
ASB1	3984	1	ENSMUSG00000026311

VIM	4027	1	ENSMUSG00000026728
SPEF1	4077	1	ENSMUSG00000027329
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FBXO44	4240	1	ENSMUSG00000029001
LIMK1	4297	1	ENSMUSG00000029674
LDHB	4340	1	ENSMUSG00000030246
SYTL2	4386	1	ENSMUSG00000030616
SH3GL3	4389	1	ENSMUSG00000030638
MSN	4434	1	ENSMUSG00000031207
IL2RG	4442	1	ENSMUSG00000031304
SLC37A2	4518	1	ENSMUSG00000032122
MCAM	4520	1	ENSMUSG00000032135
SCN5A	4554	1	ENSMUSG00000032511
ZNRF1	4599	1	ENSMUSG00000033545
WDR78	4659	1	ENSMUSG00000035126
PRICKLE1	4686	1	ENSMUSG00000036158
PPFIBP2	4698	1	ENSMUSG00000036528
BC022687	4739	1	ENSMUSG00000037594
CTNNA1	4747	1	ENSMUSG00000037815
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HLCS	4874	1	ENSMUSG00000040820
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TMEM229B	5017	1	ENSMUSG00000046157
PPP1R3B	5034	1	ENSMUSG00000046794
BTLA	5105	1	ENSMUSG00000052013
SERP2	5113	1	ENSMUSG00000052584
REEP1	5117	1	ENSMUSG00000052852
PRELID2	5181	1	ENSMUSG00000056671
BCL2A1D	5348	1	ENSMUSG00000074148
TRBV29	5368	1	ENSMUSG00000076480

Figure S1-S6

Figure S1

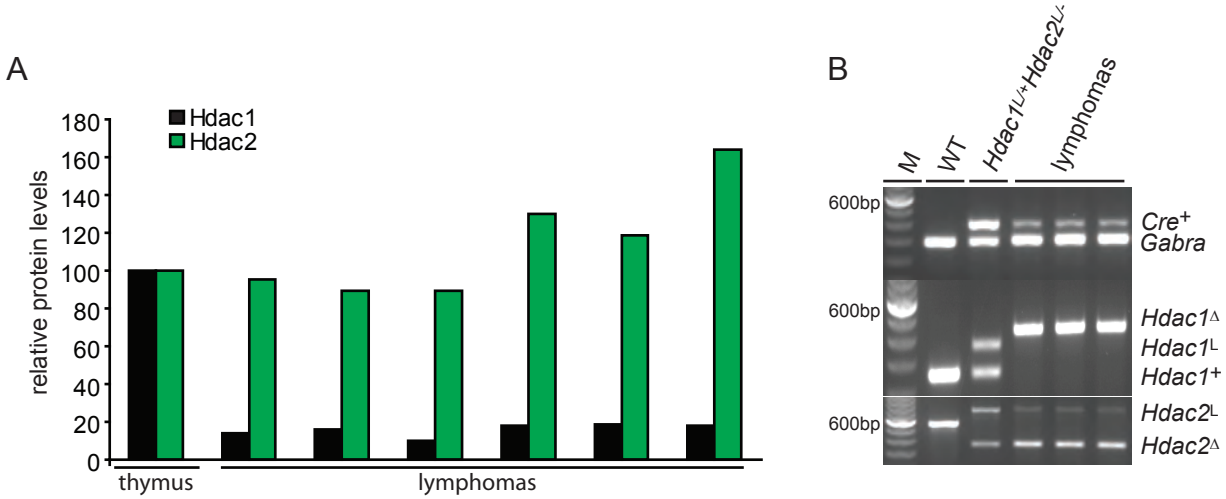

Figure S1. Dosage dependent tumorigenesis in non-induced MxCre^{+};Hdac1$^{L/L}$;Hdac2$^{L/L}$ mice. (*A*) Quantification of Hdac1 and Hdac2 western blot analysis of *wild type* (*WT*) thymus and 6 independent lymphomas from non-induced *MxCre^{+};Hdac1$^{L/L}$;Hdac2$^{L/L}$* mice. α-tubulin served as a loading control. Values are relative to Hdac1 and Hdac2 levels in *WT* thymocytes. (*B*) PCR genotype analysis of *Hdac1* and *Hdac2* alleles in tumor cell lines derived from lymphomas arising in *MxCre^{+};Hdac1$^{L/L}$;Hdac2$^{L/L}$* mice. M indicates 100bp DNA size marker.

Figure S2

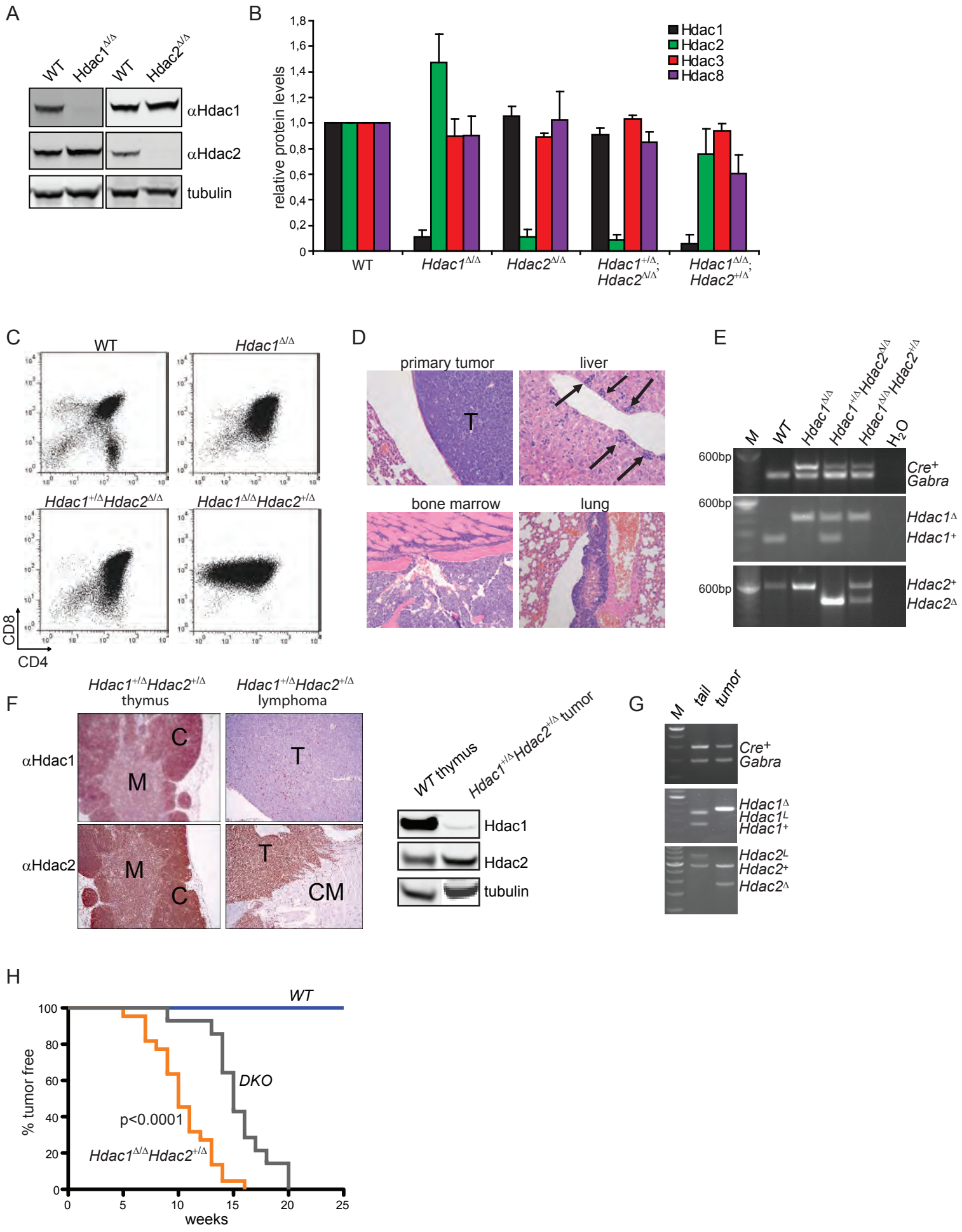
A
WT
Hdac1Δ/Δ
WT
Hdac2Δ/Δ
αHdac1
αHdac2
tubulin
B
relative protein levels
Hdac1
Hdac2
Hdac3
Hdac8
WT
Hdac1Δ/Δ
Hdac2Δ/Δ
Hdac1+/Δ; Hdac2Δ/Δ
Hdac1Δ/Δ; Hdac2+/Δ
C
WT
Hdac1Δ/Δ
Hdac1+/ΔHdac2Δ/Δ
Hdac1Δ/ΔHdac2+/Δ
CD8
CD4
D
primary tumor
liver
bone marrow
lung
T
E
M
WT
Hdac1Δ/Δ
Hdac1+/ΔHdac2Δ/Δ
Hdac1Δ/ΔHdac2+/Δ
H2O
600bp
Cre+ Gabra
Hdac1Δ
Hdac1+
Hdac2+
Hdac2Δ
F
Hdac1+/ΔHdac2+/Δ thymus
Hdac1+/ΔHdac2+/Δ lymphoma
αHdac1
αHdac2
C
M
T
CM
WT thymus
Hdac1+/ΔHdac2-/Δ tumor
Hdac1
Hdac2
tubulin
G
M
tail
tumor
Cre+ Gabra
Hdac1Δ
Hdac1L
Hdac1+
Hdac2L
Hdac2+
Hdac2Δ
H
WT
DKO
p<0.0001
Hdac1Δ/ΔHdac2+/Δ
% tumor free
weeks

Figure S2. Thymocyte specific deletion of Hdac1 and Hdac2 combinations results in dosage dependent lymphomagenesis. (*A*) Hdac1 and Hdac2 western blot analysis of *WT*, *LckCre;Hdac1*$^{\Delta/\Delta}$ and *LckCre;Hdac2*$^{\Delta/\Delta}$ thymi. α-tubulin served as a loading control. (*B*) Quantitative western blot analysis of protein lysates from thymocytes with indicated genotypes for class I Hdac1, Hdac2, Hdac 3 and Hdac8. Indicated mean values are relative to class I Hdac protein levels in *WT* thymocytes and error bars represent standard deviations of at least three independent thymi per genotype. α-tubulin served as a loading control. (*C*) Representative dot plots of a *WT* thymus and thymic lymphomas from mice with indicated genotypes analyzed by flow cytrometry using labeled CD4 and CD8 antibodies. (*D*) Representative pictures of hematoxylin-eosin stained histological sections of a primary *LckCre*$^{+}$;*Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ lymphoma (T), which disseminated to liver (arrows indicate nests of tumor cells next to a major hepatic blood vessel), bone marrow (tumor infiltrating into adjacent muscle tissue) and lung. (*E*) PCR genotype analysis of *Hdac1* and *Hdac2* alleles in tumor cell lines derived from lymphomas with indicated genotypes. *WT* thymus and no DNA (H_2O) served as a control. M indicates 100bp DNA size marker. (*F*) (left panel) Representative pictures of a Hdac1 and Hdac2 immunohistochemical analysis of a *LckCre;Hdac1*$^{+/\Delta}$;*Hdac2*$^{+/\Delta}$ thymus (left) and a lymphoma (right) dissected from a *LckCre;Hdac1*$^{+/\Delta}$;*Hdac2*$^{+/\Delta}$ mouse. C: cortex, M: medulla, T: tumor, CM: cardiac muscle. Magnification: 100x. (right panel) Hdac1 and Hdac2 western blot analysis of a *WT* thymus and from a tumor arising in a *LckCre;Hdac1*$^{+/\Delta}$;*Hdac2*$^{+/\Delta}$ mouse. α-tubulin served as a loading control. (*G*) PCR genotype analysis of *Hdac1* and *Hdac2* alleles of *WT* thymus and from a tumor arising in a *LckCre;Hdac1*$^{+/\Delta}$ *Hdac2*$^{+/\Delta}$ mouse. (*H*) Kaplan-Meier tumour free survival plot of *WT*, *LckCre;Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ and *DKO* mice. P-value was calculated using a Chi-square test.

Figure S3

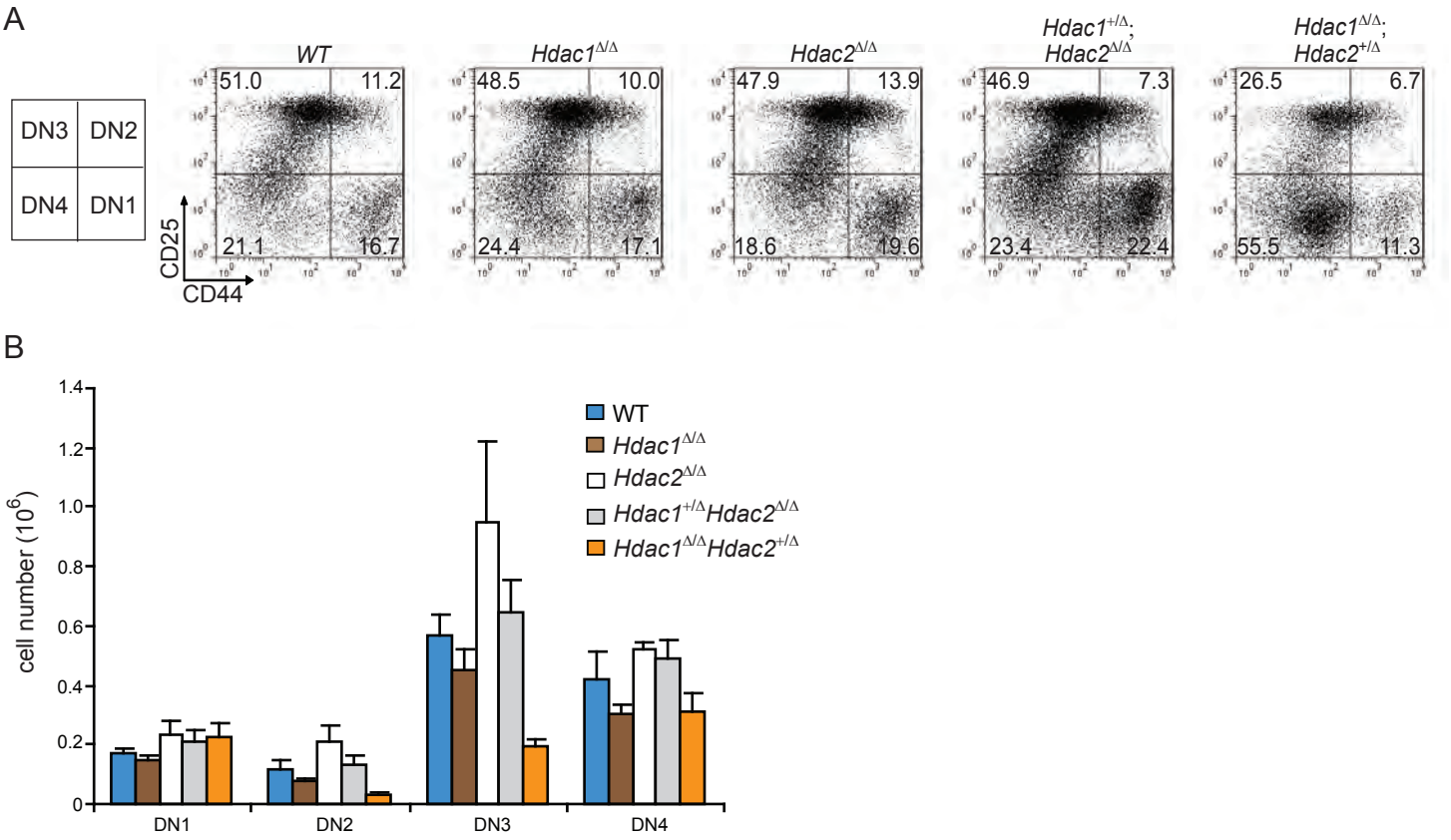

Figure S3. Early thymocyte development in compound Hdac1 and Hdac2 deficient thymocytes. (*A*) To determine the distribution of early DN thymocytes from mice with indicated genotypes, thymocytes were isolated and stained with labeled antibodies against Thy1, CD4, CD8, CD25, CD44 and analyzed by flow cytometry. Thy1+CD4-CD8- cells were gated and plotted for CD25 and CD44. $CD25^{-}CD44^{+}$ = DN1; $CD25^{+}CD44^{+}$ = DN2; $CD25^{+}CD44^{-}$ = DN3; $CD25^{-}CD44^{-}$ = DN4. Representative percentages of thymocyte subpopulations are indicated in the quadrants. (*B*) Absolute numbers of DN1, DN2, DN3 and DN4 thymocyte populations in thymi from mice with indicated genotypes. Error bars indicate standard deviations of at least 3 independent mice per genotype.

Figure S4

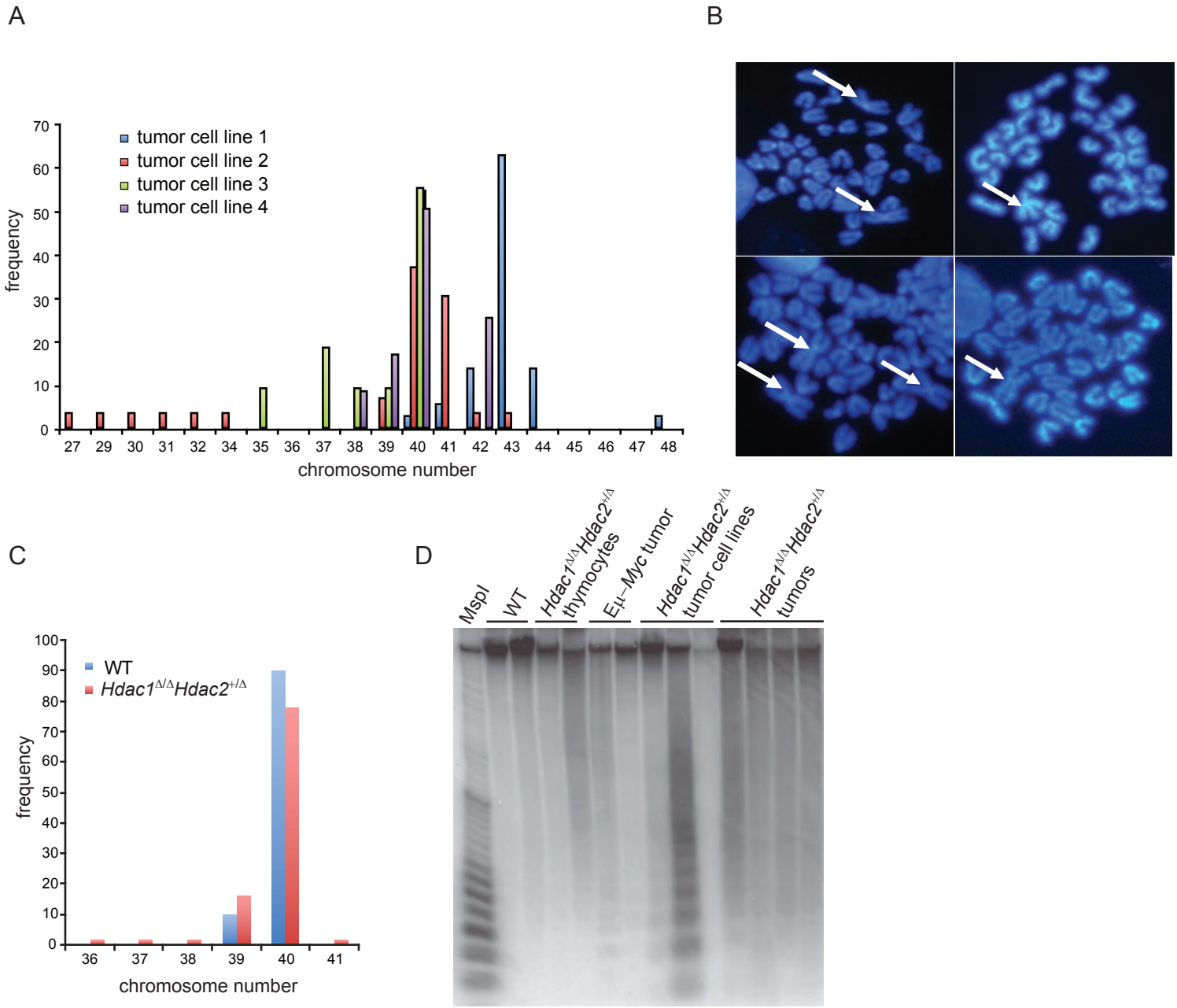

Figure S4. Absence of acute chromosomal instability and centromeric hypomethylation in *LckCre;Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ thymocytes and tumors. (*A*) Quantification of chromosome number in metaphase spreads from four independent *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ tumor cell lines indicated a near diploid genome. (*B*) Representative pictures of metaphase spreads from four independent *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ tumor cell lines. White arrows indicate centromeric attachment of chromosomes. (*C*) Average chromosome numbers in metaphase spreads of four independent colcemid treated one week old *WT* and *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ pre-leukemic thymocyte cultures. (*D*) Centromeric repeat methylation of *WT* and pre-leukemic *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ thymocytes, *Eμ-Myc* and *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ tumor cell lines and *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{+/\Delta}$ primary tumors analyzed by Southern blot analysis using a probe recognizing centromeric major satellite repeats. Genomic DNA digested with the DNA methylation insensitive *Msp1* restriction enzyme served as positive control.

Figure S5

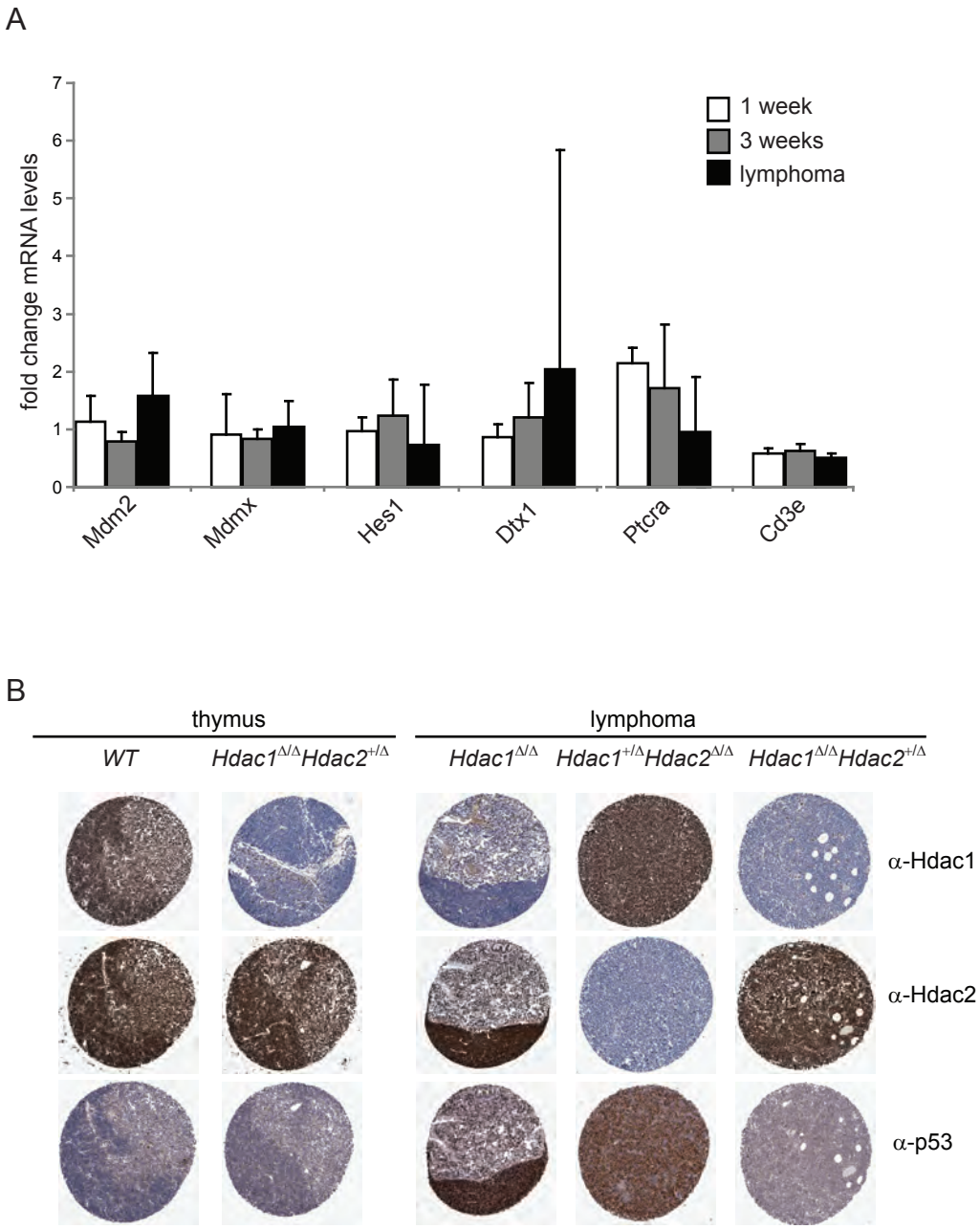

Figure S5. Gradual loss of Hdac1 and Hdac2 results in alleviation of p53 inactivation during lymphomagenesis. (*A*) Fold changes of p53 regulators *Mdm2 and Mdmx*, Notch targets *Hes1*, *Dtx1*, *Ptcra* and *Cd3*ε, in one and three week old *Hdac1* $^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ thymocytes and *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ lymphomas, relative to agematched wild-type thymi. (*B)* Representative pictures of immunohistochemical analysis of p53 status in a tissue micro-array containing three weeks old *WT* and *Hdac1* $^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ thymi and *Hdac1*$^{+/\Delta}$;*Hdac2*$^{\Delta/\Delta}$ (n=4) *Hdac1*$^{\Delta/\Delta}$ (n=5) and *Hdac1*$^{\Delta/\Delta}$;*Hdac2*$^{+/\Delta}$ (n= 36) lymphomas. Hdac1 and Hdac2 staining was used to confirm expression status of Hdac1 and Hdac2 in tumors with indicated genotypes.

Figure S6

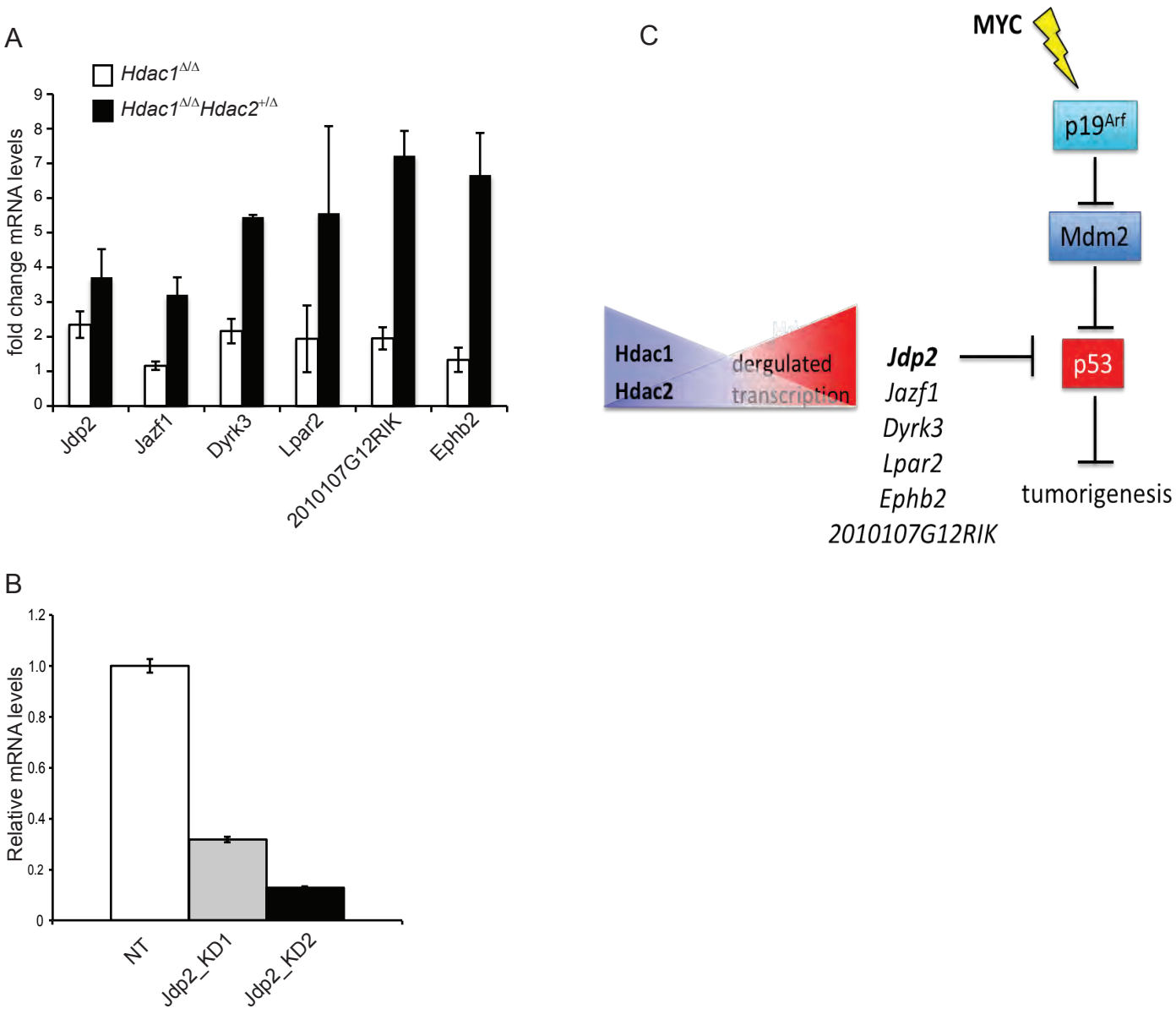

Figure S6. Hdac1 and Hdac2 dosage dependent regulation of p53-suppressing genes. (*A*) Fold changes in Jdp2, Jazf1, Dyrk3, Lpar2, 1190002H23RIK and Ephb2 in *Hdac1*$^{\Delta/\Delta}$ and *Hdac1*$^{\Delta/\Delta}$*;Hdac2*$^{\Delta/+}$ pre-leukemic thymocytes. (*B*) Histogram showing Jdp2 knock-down efficiency determined by qPCR of 2 independent lentiviral shRNA constructs compared to a non-targeting (NT) shRNA construct and normalized by Gapdh levels in wild-type MEFs. (*C*) Working model for Hdac1 and Hdac2 mediated tumor suppression. Hdac1 and Hdac2 collectively regulateexpression of numerous genes including Myc-collaborating, p53-suppressing genes in a dosage dependent manner. Partial loss of HDAC1 and HDAC2 results in derepression of Jdp2, Dyrk3 and Lpar2 among others and causes suppression of the p53-dependent tumor protective pathwayunleashing the oncogenic potential of Myc. In addition HDAC1 and HDAC2 may have p53-independent functions in tumor suppression.