SUPPLEMENTAL TABLES

Supplemental Table 1: List of proteins identified by mass spectrometry.

#	Symbol	Characteristics of proteins	Accession number	Molecular weight (kDa)	Unique peptides
1	DHX9	ATP-dependent RNA helicase A	Q08211	141	41
2	MYBBP1A	Myb-binding protein 1A	Q9BQG0	149	32
3	ADAR	Adenosine deaminase, RNA-specific	Q59EC0	138	31
4	LMNA	Prelamin-A/C	P02545	74	31
5	SMC1A	Structural maintenance of chromosomes protein 1A	Q14683	143	30
6	DDX21	Nucleolar RNA helicase 2	Q9NR30	87	27
7	HNRNPU	Heterogeneous nuclear ribonucleoprotein U	Q00839	91	25
8	ILF3	Interleukin enhancer-binding factor 3	Q12906	95	23
9	SF3B1	Splicing factor 3B subunit 1	O75533	146	23
10	HNRNPM	Heterogeneous nuclear ribonucleoprotein M	P52272	78	22
11	VIM	Vimentin	P08670	54	22
12	DDX24	ATP-dependent RNA helicase DDX24	Q9GZR7	96	22
13	NCL	Nucleolin	P19338	77	20
14	KHSRP	Far upstream element-binding protein 2	Q92945	73	20
15	TOP2B	DNA topoisomerase 2-beta	Q02880	183	20
16	NONO	Non-POU domain-containing octamer-binding protein	Q15233	54	19
17	SF3B2	Splicing factor 3B subunit 2	Q13435	100	18
18	PRKDC	DNA-dependent protein kinase catalytic subunit	P78527	469	17
19	DDX17	DEAD box polypeptide 17 isoform p82 variant	Q59F66	81	16
20	HNRNPR	Heterogeneous nuclear ribonucleoprotein R	O43390	71	16
21	PARP1	Poly [ADP-ribose] polymerase 1	P09874	113	16
22	HNRNPK	Heterogeneous nuclear ribonucleoprotein K	P61978	51	16
23	SFPQ	Splicing factor, proline- and glutamine-rich	P23246	76	15
24	SMARCA5	SWI/SNF-related matrix-associated actin-	O60264	122	15

		dependent regulator of chromatin subfamily A member 5			
25	GNL3	Guanine nucleotide-binding protein-like 3	Q9BVP2	62	15
26	HP1BP3	Heterochromatin protein 1-binding protein 3	Q5SSJ5	61	14
27	HNRNPL	Heterogeneous nuclear ribonucleoprotein L	P14866	64	13
28	IFI16	Gamma-interferon-inducible protein Ifi-16	B4DJT8	83	13
29	PES1	Pescadillo homolog	O00541	68	13
30	XRCC6	X-ray repair cross-complementing protein 6	P12956	70	13
31	SYNCRIP	Heterogeneous nuclear ribonucleoprotein Q	O60506	70	12
32	ZFR	Zinc finger RNA-binding protein	Q96KR1	117	12
33	NUMA1	Nuclear mitotic apparatus protein 1	Q14980	238	12
34	HNRNPC	Heterogeneous nuclear ribonucleoproteins C1/C2	P07910	34	12
35	RRP12	RRP12-like protein	Q5JTH9	144	12
36	DDX5	Probable ATP-dependent RNA helicase DDX5	P17844	69	12
37	PRPF6	Pre-mRNA-processing factor 6	O94906	107	12
38	RAD50	DNA repair protein RAD50	Q92878	154	12
39	STRBP	Spermatid perinuclear RNA-binding protein	Q96SI9	74	11
40	ILF2	Interleukin enhancer-binding factor 2	Q12905	43	11
41	PBRM1	Protein polybromo-1	Q86U86	193	11
42	DDX18	ATP-dependent RNA helicase DDX18	Q9NVP1	75	11
43	HSP90AB1	Heat shock protein HSP 90-beta	P08238	83	11
44	PDS5A	Sister chromatid cohesion protein PDS5 homolog A	Q29RF7	151	11
45	BAZ1B	Tyrosine-protein kinase BAZ1B	Q9UIG0	171	10
46	TMPO	Lamina-associated polypeptide 2, isoform alpha	P42166	75	10
47	NOP56	Nucleolar protein 56	O00567	66	10
48	LMNB1	Lamin-B1	P20700	66	10
49	SF3B3	Splicing factor 3B subunit 3	Q15393	136	10
50	EZR	Ezrin	P15311	69	10
51	HNRNPH1	Heterogeneous nuclear	P31943	49	10

		ribonucleoprotein H			
52	XRCC5	X-ray repair cross-complementing protein 5	P13010	83	10
53	CDC5L	Cell division cycle 5-like protein	Q99459	92	10
54	PTBP1	Polypyrimidine tract-binding protein 1	P26599	57	9
55	HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	P51991	40	9
56	RPN1	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	P04843	69	9
57	MECP2	Methyl-CpG-binding protein 2	P51608	52	9
58	PDCD11	Protein RRP5 homolog	Q14690	209	9
59	DHX37	Probable ATP-dependent RNA helicase DHX37	Q8IY37	130	9
60	PRPF19	Pre-mRNA-processing factor 19	Q9UMS4	55	9
61	HSPD1	60 kDa heat shock protein, mitochondrial	P10809	61	9
62	TOP1	DNA topoisomerase 1	P11387	91	9
63	DDX1	ATP-dependent RNA helicase DDX1	Q92499	82	9
64	RUVBL2	RuvB-like 2	Q9Y230	51	9
65	UTP3	Something about silencing protein 10	Q9NQZ2	55	8
66	HNRNPD	Heterogeneous nuclear ribonucleoprotein D0	Q14103	38	8
67	RBM10	RNA-binding protein 10	P98175	104	8
68	CSTF3	Cleavage stimulation factor subunit 3	Q12996	83	8
69	POP1	Ribonucleases P/MRP protein subunit POP1	Q99575	115	8
70	GPATCH4	G patch domain-containing protein 4	Q5T3I0	50	7
71	TOR1AIP1	Torsin-1A-interacting protein 1	Q5JTV8	66	7
72	SMARCA4	Transcription activator BRG1	P51532	185	7
73	ATP5B	ATP synthase subunit beta, mitochondrial	P06576	57	7
74	PSPC1	Paraspeckle component 1	Q8WXF1	59	7
75	HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	P09651	39	7
76	RBMX	Heterogeneous nuclear ribonucleoprotein G	P38159	42	7
77	SART3	Squamous cell carcinoma antigen recognized by T-	Q15020	110	7

		cells 3			
78	PKP2	Plakophilin 2	A0AV37	93	7
79	POLR1A	DNA-directed RNA polymerase I subunit RPA1	O95602	195	7
80	ACTB	Actin, cytoplasmic 1	P60709	42	7
81	TBL3	Transducin beta-like protein 3	Q12788	89	7
82	HNRNPUL2	Heterogeneous nuclear ribonucleoprotein U-like protein 2	Q1KMD3	85	7
83	DDX54	ATP-dependent RNA helicase DDX54	Q8TDD1	99	7
84	NOL10	Nucleolar protein 10	Q9BSC4	80	7
85	SDAD1	Protein SDA1 homolog	Q9NVU7	80	7
86	CHERP	Calcium homeostasis endoplasmic reticulum protein	Q8IWX8	104	6
87	EWSR1	RNA-binding protein EWS	Q01844	68	6
88	FUS	RNA-binding protein FUS	P35637	53	6
89	KIAA1967	Protein KIAA1967	Q8N163	103	6
90	ARHGAP4	Rho GTPase-activating protein 4	P98171	105	6
91	HADHA	Trifunctional enzyme subunit alpha, mitochondrial	P40939	83	6
92	RRP1	Ribosomal RNA processing protein 1 homolog A	P56182	53	6
93	DDX31	Probable ATP-dependent RNA helicase DDX31	Q9H8H2	94	6
94	NOP58	Nucleolar protein 58	Q9Y2X3	60	6
95	HNRPAB	Homo sapiens heterogeneous nuclear ribonucleoprotein A/B (HNRPAB), transcript variant 1, mRNA	B4DMY3	35	6
96	PSIP1	PC4 and SFRS1-interacting protein	O75475	60	6
97	DDX50	ATP-dependent RNA helicase DDX50	Q9BQ39	83	6
98	CDKN2AIP	CDKN2A-interacting protein	Q9NXV6	61	6
99	NOLC1	Nucleolar and coiled-body phosphoprotein 1	Q14978	74	5
100	PCF11	Pre-mRNA cleavage complex 2 protein Pcf11	O94913	173	5
101	RANGAP1	Ran GTPase-activating protein 1	P46060	64	5
102	RBM25	RNA-binding protein 25	P49756	100	5
103	SF3A1	Splicing factor 3A subunit	Q15459	89	5

		1			
104	SUN2	SUN domain-containing protein 2	Q9UH99	80	5
105	GTF3C4	General transcription factor 3C polypeptide 4	Q9UKN8	92	5
106	PLRG1	Pleiotropic regulator 1	O43660	57	5
107	NUP93	Nuclear pore complex protein Nup93	Q8N1F7	93	5
108	RAVER1	Ribonucleoprotein PTB-binding 1	Q8IY67	64	5
109	MPHOSPH10	U3 small nucleolar ribonucleoprotein protein MPP10	O00566	79	5
110	RBBP4	Histone-binding protein RBBP4	Q09028	48	5
111	CD3EAP	DNA-directed RNA polymerase I subunit RPA34	O15446	55	5
112	USP39	U4/U6.U5 tri-snRNP-associated protein 2	Q53GS9	65	5
113	HDLBP	Vigilin	Q00341	141	5
114	HSD17B4	Peroxisomal multifunctional enzyme type 2	P51659	80	5
115	TARDBP	TAR DNA-binding protein 43	Q13148	45	5
116	RBM14	RNA-binding protein 14	Q96PK6	69	5
117	AATF	Protein AATF	Q9NY61	63	5

Supplemental Table 2: Network function analysis of proteins binding to ACA11.

ID	Molecules in Network	Score	Focus Molecules	Top Functions
1	ADAR, BAZ1B, DDX5, DDX17, DDX21, DHX9, HNRNPC, HNRNPD, HNRNPH1, HNRNPK, HNRNPL, HNRNPM, HNRNPR, HNRNPU, IFI16, ILF3, ILF2, KHSRP, Lamin b, LMNA, LMNB1, NCL, NONO, PARP1, PDS5A, PRKDC, PTBP1, SFPQ, SYNCRIP, TOP2B	77	30	RNA Post-Transcriptional Modification, Gene Expression, Infection Mechanism
2	DDX18, DDX24, GNL3, HSP90AB1, NUMA1, RAD50, SF3B1, SF3B2, SF3B3, SMARCA5, SMC1A, STRBP, UTP3	27	13	Embryonic Development, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair
3	EZR, HNRNPA3, MYBBP1A, NOP56, PBRM1, PES1, PRPF6, RRP12, TMPO, VIM, ZFR	22	11	Neurological Disease, Lipid Metabolism, Small Molecule Biochemistry

The table contains columns with the network number, the names of the proteins involved in the network, the score value and the top functions. The top functions with score > 20 were listed.

Supplemental Table 3: ILF3 immunoprecipitation deep sequencing peaks from H929 myeloma cells.

Chr	Start	Stop	Gene ID	Tags
chr17	33477970	33478302	UNC45B	331879
chr1	564294	570463	Pseudogenes	215840
chr17	27050446	27051850	RPL23A	170847
chr4	1976359	1977583	SCARNA22	149143
chr19	51305209	51305945	SNORD88C	50576
chr5	180669835	180670898	SNORD95	45082
chr9	35657573	35658028	RMRP	39351
chr12	49047633	49048307	SNORA34	36299
chr6	86386577	86388452	SNORD50A/B	30509
chr19	17972750	17974267	RPL18A	30256
chr15	65588030	65589356	RNU5A	28263
chr13	92002357	92004259	lincRNA/miRNA	26741
chr5	93903713	93905537	KIAA0825	21434
chr2	149639151	149639580	KIF5C	21106
chr17	19092523	19093559	SNORD3C	14836
chr5	134258935	134264319	PCBD2	14740
chr17	27047253	27048223	RPL23a	12577
chr11	62432719	62433383	SNORA57	11323
chr3	52725390	52725804	SNORD19.1	11295
chr17	7479512	7482522	SNORD10	10714
chr5	60057208	60057576	ELOVL7	10704
chr17	74554508	74555419	SNORD1C	10206
chr2	89155530	89157882	IGKC	9958
chr22	39714874	39715416	RPL3	9929
chr6	26156556	26159443	HIST1H1E	7650
chrX	153626578	153629796	RPL10	5959
chr1	161409744	161410046	tRNA	5524
chr15	65597014	65597571	RNU5B-1	4971
chr1	149856801	149860791	HIST2H2BE	4911
chr17	79476814	79479417	ACTG1	4791
chr15	25330380	25330799	SNORD116-18	4719
chr15	25296283	25296860	SNORD116-1	4698
chr12	7076176	7077290	PHB2	4600
chr8	101729524	101731076	PABPC1	4426
chr15	25339184	25339448	SNORD116-24	4425
chr11	65266516	65274171	MALAT1	4140
chr1	149679895	149680702	tRNA	4081
chr15	45492151	45492730	tRNA	3945
chr11	68227166	68227703	Pseudogenes	3780
chr6	27860000	27860962	HIST1H2AM	3758
chr14	102550579	102552728	HSP90AA1	3725
chr6	74226861	74230298	EEF1A1	3697
chr5	99381740	99382414	Pseudogenes	3685
chr20	37061977	37062996	SNORA71D	3630
chr15	25335070	25335326	SNORD116-22	3478

chr16	2010800	2013254	RPS2	3446
chr17	41464449	41464974	RNU2-4P	3343
chr12	112704597	112705271	7SK.58	3262
chr11	27909546	27912612	Pseudogenes	3050
chr15	25351284	25351911	SNORD116-29	2929

Top 50 enriched peaks (pull-down versus input) by number of sequence tags. Chr, chromosome number; Gene ID, HGNC Symbol. Coordinates listed are based upon human genome assembly GRCh39/hg19.

Supplemental Table 4: Genes significantly dysregulated specifically in 4p16 subtype, compared to 5 other major subtypes.

Probe set ID	4p16 vs. D2	4p16 vs. D1+D2	4p16 vs. MAF	4p16 vs. D1	4p16 vs. 11q13	Gene symbol	Chromosome location
1557780_at	8.815170521	8.227863196	7.915054774	8.695246881	7.789189389	NA	NA
209052_s_at	11.87530979	12.11755821	10.08957466	12.44266003	10.71741204	WHSC1	4p16.3
209053_s_at	26.52188818	27.34280811	15.40828333	28.47863657	19.39515913	WHSC1	4p16.3
209054_s_at	10.62433479	10.41839947	8.466851726	11.53095477	8.866102081	WHSC1	4p16.3
211709_s_at	2.445295292	2.812534411	2.62452927	2.69840074	2.757718771	CLEC11A	19q13.3
217901_at	6.440010094	7.537449546	11.27697576	8.226886552	7.465536199	DSG2	18q12.1
222777_s_at	33.19548125	29.33012687	24.8285743	29.88648636	24.65156524	WHSC1	4p16.3
222778_s_at	14.00362924	13.0218553	13.55580564	15.66522887	11.95288327	WHSC1	4p16.3
223472_at	18.89567231	19.07338158	19.01779111	19.36068639	15.9127712	WHSC1	4p16.3
225530_at	0.24755202	0.200473517	0.122993653	0.183763481	0.204005076	MOBKL2A	19p13.3
236565_s_at	2.546004331	2.706020348	2.785394759	2.647020301	2.750105773	LARP6	15q23
238012_at	0.270036646	0.316268589	0.251063552	0.327721352	0.317594463	DPP7	9q34.3
214464_at	4.306084946	4.658893574	3.888346541	4.516948218	4.573322929	CDC42BPA	1q42.11
220266_s_at	8.553007833	8.184115744	5.416095438	6.520860238	6.741678726	KLF4	9q31
1553105_s_at	4.399273258	4.801983384	6.397106238	5.421413173	4.721582823	DSG2	18q12.1
205131_x_at	1.675377853	1.749206524	1.715729667	1.713043323	1.765391146	CLEC11A	19q13.3
223313_s_at	3.214420707	3.755610794	2.995796185	3.934112949	1.934120458	NA	NA
204379_s_at	53.10680846	44.16169171	52.53577134	52.10784015	51.66151385	FGFR3	4p16.3
227084_at	2.214427653	2.203161014	2.602520447	2.250684408	2.496368547	DTNA	18q12
210220_at	2.322378538	2.116120445	3.120458066	2.404499858	2.299781936	FZD2	17q21.1
201911_s_at	1.591800943	1.903426713	1.598952555	1.783279705	1.62155216	FARP1	13q32.2
217867_x_at	2.082503273	2.425476828	2.40008601	2.486016021	2.497593397	BACE2	21q22.3
242311_x_at	1.658540194	1.597445734	1.562988446	1.591237229	1.435965538	NA	NA
229344_x_at	1.671920494	1.643507507	1.826168489	1.683433657	1.60725015	RIMKLB	12p13.31
221261_x_at	4.493010097	5.86338116	3.475028669	5.905433063	2.032994351	NA	NA
222372_at	2.055266249	2.245334343	2.58871626	2.324751555	2.640498956	NA	NA
41220_at	0.606076458	0.5415375	0.384938722	0.450240775	0.399026387	SEPT9	17q25
207233_s_at	2.610627877	2.717029621	1.927748421	3.297512897	3.035929294	MITF	3p14.2-p14.1
204749_at	2.328954513	3.253976627	2.985813743	3.04958246	2.560164373	NAP1L3	Xq21.3-q22
201360_at	3.571902014	6.435774117	5.0850233	6.622779026	4.802183961	CST3	20p11.21
200897_s_at	2.738177869	2.399571804	3.01144564	2.902145484	2.589543608	PALLD	4q32.3
240125_at	1.618797757	1.564557023	1.753359165	1.627217017	1.618095725	NA	NA
212372_at	3.495461628	3.055882005	4.889829599	4.20992056	4.248552251	MYH10	17p13
218675_at	2.610414754	2.795993633	3.361038028	2.617254842	1.874795772	SLC22A17	14q11.2
221841_s_at	23.73227007	19.1701072	9.69666219	12.43933921	14.78790003	KLF4	9q31
219122_s_at	0.415633849	0.392098226	0.49208587	0.272952546	0.622515156	THG1L	5q33.3
223821_s_at	1.577888723	1.725730591	1.723538057	1.67261502	1.679422425	SUSD4	1q41
233240_at	2.841677202	2.922287507	3.036377197	2.637939912	2.114802354	NA	NA
212771_at	3.605468743	3.019918804	7.596879137	4.281159484	10.0760003	FAM171A1	10p13
201910_at	1.483881895	1.484876423	1.598675179	1.542445789	1.503481568	FARP1	13q32.2
227290_at	1.509740162	1.570809544	1.545073093	1.535588075	1.519692773	NA	NA
210783_x_at	1.37678931	1.471427636	1.535083359	1.45041143	1.471468229	CLEC11A	19q13.3
218775_s_at	1.855061846	1.740861651	1.989558761	1.875312265	1.720081117	WWC2	4q35.1
205573_s_at	2.458978011	2.706439419	2.570775024	2.485169006	1.849952702	SNX7	1p21.3
200981_x_at	1.480935971	1.531422695	1.865977484	1.732854411	1.305536928	GNAS	20q13.3
200780_x_at	1.483881618	1.574185143	1.872610089	1.765714699	1.313067632	GNAS	20q13.3
238569_at	1.414373539	1.630058525	1.541833484	1.622661338	1.608863855	GABBR1	6p21.31
200907_s_at	2.021629851	1.80283166	2.235581799	1.973906585	1.92715494	PALLD	4q32.3
204380_s_at	7.356094478	7.003862142	7.574083189	7.427997251	7.526320805	FGFR3	4p16.3
204121_at	2.013302357	1.956067147	1.788163484	2.052116062	2.124034456	GADD45G	9q22.1-q22.2
201922_at	0.527308371	0.473108209	0.659293637	0.437535357	0.636784339	NSA2	5q13.3
204518_s_at	3.047652254	2.78655103	2.958807567	3.622497052	3.756292903	PPIC	5q23.2
228237_at	1.379254759	1.465733561	1.576070022	1.481044226	1.608392657	PAPPA2	1q23-q25
222738_at	1.437051237	1.472277721	1.44535218	1.467141244	1.353009985	WWC2	4q35.1
214548_x_at	1.523469448	1.562387857	1.978121224	1.795069257	1.357703839	GNAS	20q13.3
222446_s_at	1.655946344	1.949049557	1.837119143	1.884637364	1.89795244	BACE2	21q22.3
219631_at	2.185049559	2.552666262	2.964170266	2.28757194	2.338804217	LRP12	8q22.2-q23.1
212273_x_at	1.481867708	1.553894386	1.860832308	1.763823283	1.308655351	GNAS	20q13.3
217807_s_at	0.564801118	0.492401268	0.504572797	0.381614485	0.533354714	GLTSCR2	19q13.3
226313_at	1.399131145	1.51492661	1.649587526	1.397606891	1.348005457	C10orf35	10q22.1
203794_at	1.467182588	1.601629096	1.440519918	1.520166624	1.585593711	CDC42BPA	1q42.11
205011_at	2.108086178	2.155855803	1.798362011	2.760624974	1.744459448	VWA5A	11q23

212190_at	9.916491953	6.95380817	9.084570422	6.15741251	4.778067922	SERPINE2	2q33-q35
227641_at	0.364489004	0.306388394	0.590063553	0.443972378	0.318980266	FBXL16	16p13.3
225698_at	0.429111013	0.440137946	0.543468787	0.290775996	0.512081746	NCRNA00219	5q21-q22
224572_s_at	2.174035588	2.364066986	1.831363847	2.77072684	1.548876796	IRF2BP2	1q42.3
219550_at	1.517965013	1.730428147	1.840703762	1.642775746	1.972088912	ROBO3	11q24.2
212813_at	1.801500508	1.782484934	2.223439735	2.028195471	2.081992568	JAM3	11q25
238116_at	1.656342465	1.751474691	1.804894032	1.703936579	1.751551163	DYNLRB2	16q23.3
1554762_a_at	1.394923648	1.419460048	1.622613794	1.415022308	1.387706311	WWC2	4q35.1
1557803_at	2.051290585	2.144233387	2.271673665	2.096588289	2.25966435	NA	NA
232235_at	3.754473483	4.807719855	4.471475241	3.878046489	2.637620077	DSEL	18q22.1
233792_at	1.59030715	1.685577968	1.609730477	1.58963361	1.421357116	NA	NA
204066_s_at	2.863165963	2.528657242	2.636361951	2.912723019	3.869079129	AGAP1	2q37
228745_at	0.43827529	0.422720626	0.35528796	0.448360848	0.438922867	SGTB	5q12.3
225536_at	1.345171489	1.439143738	1.710364668	1.430636068	1.487784593	TMEM54	1p35-p34
227195_at	2.33941018	2.186592118	2.821924182	2.534775033	2.9606179	ZNF503	10q22.2
217673_x_at	1.305922798	1.354887988	1.746366822	1.540131242	1.271760393	GNAS	20q13.3
204069_at	1.606703726	1.80496345	1.718372592	1.677370695	1.673494558	MEIS1	2p14-p13
239297_at	1.739233203	1.905918642	2.154991646	1.980757679	2.006310501	C8orf79	8p22
1556545_at	4.230664582	3.880388896	12.83385401	3.586528409	2.153619717	NA	NA
212504_at	1.397079953	1.537876584	1.666068587	1.442809037	1.544875383	DIP2C	10p15.3
235501_at	1.838236733	1.955521157	1.708503782	1.928779076	1.590628788	NA	NA
230941_at	1.517926086	1.561051927	1.624238583	1.487662045	1.554513007	LOC728537	2q11.2
219389_at	1.222757162	1.374154155	1.320110507	1.283825028	1.331217945	SUSD4	1q41
211276_at	3.357813263	3.501630374	2.883217407	3.391335976	1.880400392	TCEAL2	Xq22.1-q22.3
202105_at	0.631590829	0.634122403	0.659709972	0.555383203	0.601516352	IGBP1	Xq13.1-q13.3
200809_x_at	0.689273813	0.668748261	0.719254344	0.645730009	0.719286597	RPL12	9q34
1563881_at	1.204775797	1.245064452	1.352605677	1.272772384	1.338773045	NA	NA
200819_s_at	0.706314508	0.670207139	0.805241712	0.667823352	0.841297473	RPS15	19p13.3
1566539_at	1.248240854	1.297327657	1.396379855	1.312821498	1.378588357	NA	NA
221582_at	2.403166785	2.807523088	4.411791222	3.153626022	3.081966291	HIST3H2A	1q42.13
226164_x_at	1.356015272	1.366580196	1.322263084	1.346309146	1.271210239	RIMKLB	12p13.31
223279_s_at	1.48752948	1.636445456	2.019243404	1.876286616	2.240444312	UACA	15q22-q24
244397_at	2.060544578	2.258819729	2.73326456	1.68628017	1.662707719	NA	NA
232859_s_at	1.221248708	1.284972145	1.497066389	1.308597958	1.40559385	MAGI1	3p14.1
207585_s_at	0.641312297	0.559386445	0.660465702	0.587363999	0.593841807	RPL36AL	14q21
207321_s_at	2.055980435	2.902913467	2.259314972	2.605038472	1.693951792	ABCB9	12q24
223822_at	1.448940727	1.586222312	1.426062081	1.547568902	1.5412525	SUSD4	1q41
211858_x_at	1.442396514	1.555142171	1.917694325	1.751850238	1.338182068	GNAS	20q13.3
218651_s_at	1.52944239	1.619645302	1.562172771	1.538901613	1.611826932	LARP6	15q23
224569_s_at	1.918235487	1.946592158	1.54464306	2.529824125	1.369656483	IRF2BP2	1q42.3
203952_at	1.483008824	1.96262961	1.969289597	2.078577821	1.770625334	ATF6	1q22-q23
211776_s_at	1.297870324	1.341228754	1.319344926	1.276999593	1.239040167	EPB41L3	18p11.32
236899_at	2.083313834	2.069534422	2.023762367	2.061108353	1.613251784	NA	NA
220254_at	1.510742359	1.71077259	1.80604258	1.629718796	1.602701462	LRP12	8q22.2-q23.1
226771_at	1.601002078	2.068365132	1.650863631	2.085364577	2.147208767	ATP8B2	1q21.3
201037_at	1.744183325	1.87895871	2.029520498	1.846473119	1.750883372	PFKP	10p15.3-p15.2
205741_s_at	1.337295448	1.369870411	1.400082623	1.36600872	1.371896935	DTNA	18q12
200091_s_at	0.715370904	0.680802729	0.719462518	0.626401197	0.720190234	RPS25	11q23.3
240255_at	1.30256069	1.440254433	1.454492023	1.295805397	1.383258777	NA	NA
227341_at	1.79449737	1.944961648	1.87393896	1.861628224	1.809993015	BEND7	10p13
218495_at	0.639928943	0.71927346	0.760376263	0.729499871	0.680676933	UXT	Xp11.23-p11.22
200926_at	0.776312217	0.747309097	0.750463705	0.717631437	0.792970629	RPS23	5q14.2
203667_at	0.69429378	0.592331839	0.68769305	0.639306329	0.849847217	TBCA	5q14.1
205975_s_at	2.037758031	2.318716722	2.663365871	2.372046781	2.529421367	HOXD1	2q31.1
224935_at	0.548840496	0.492715545	0.553551003	0.631230505	0.729048776	EIF2S3	Xp22.2-p22.1
221798_x_at	0.620195286	0.616412153	0.728513482	0.595383055	0.66952806	RPS2	16p13.3
200012_x_at	0.73622738	0.680049267	0.808057447	0.637289065	0.718583439	RPL21	13q12.2
218510_x_at	1.372219197	1.393879898	1.414540856	1.455742597	1.412131564	FAM134B	5p15.1
222651_s_at	1.391252515	1.371202779	1.356389808	1.474706783	1.279242235	TRPS1	8q24.12
204042_at	1.459167082	1.409868148	1.380839584	1.394814047	1.36078693	WASF3	13q12
201215_at	2.298496921	2.69410256	2.555010135	2.618187084	2.661151679	PLS3	Xq23
202708_s_at	3.053372951	4.932384266	6.324854872	3.006196136	1.852429756	HIST2H2BE	1q21-q23
200814_at	0.752223252	0.681057245	0.671002742	0.70522953	0.704645056	PSME1	14q11.2
200088_x_at	0.717343214	0.696728448	0.732115784	0.66532209	0.733141638	RPL12	9q34
229050_s_at	0.568782617	0.52883982	0.658661776	0.378406262	0.692032424	NA	NA
229797_at	1.249075724	1.307066292	1.38422545	1.311931492	1.276699759	MCOLN3	1p22.3
1557014_a_at	1.206526552	1.294008237	1.27220248	1.252993558	1.245498755	C9orf122	9p13.1
239246_at	1.593166142	1.652120199	1.551898273	1.64868484	1.481107807	FARP1	13q32.2
230134_s_at	0.630879075	0.615614499	0.731792185	0.652013829	0.778760771	RC3H2	9q34

214317_x_at	0.738095045	0.748892398	0.811692218	0.645760153	0.796509432	RPS9	19q13.4
1553998_at	1.860484403	1.988053527	1.900284392	1.811597329	1.511358311	NA	NA
230748_at	0.451323601	0.272412143	0.417675435	0.22859083	0.415459629	SLC16A6	17q24.2
215047_at	2.040813971	2.295159414	1.899655302	1.988168391	2.174279791	TRIM58	1q44
225474_at	1.294972837	1.423683845	1.502925853	1.353763651	1.40543924	MAGI1	3p14.1
1554420_at	2.532568554	2.555045369	3.188827709	2.636065416	1.77834286	ATF3	1q32.3
200715_x_at	0.484849614	0.458540626	0.569147033	0.332955005	0.630884622	RPL13A	19q13.3
1405_i_at	3.069401505	2.973393576	2.76858801	2.256691915	1.713478117	CCL5	17q11.2-q12
237086_at	3.572787988	3.873899095	3.633361491	3.451992872	3.596803821	FOXA1	14q12-q13
215440_s_at	3.11286201	5.927024046	3.108304642	3.434632407	1.997215474	BEX4	Xq22.1-q22.3
221726_at	0.51146524	0.524081282	0.65276439	0.432928488	0.555842856	RPL22	1p36.3-p36.2
217256_x_at	0.64813777	0.616975326	0.791687956	0.634057727	0.826972058	RPL36A	Xq22.1
201258_at	0.724366323	0.6807848	0.710192267	0.622765756	0.70427638	RPS16	19q13.1
212790_x_at	0.784727629	0.724386762	0.737297161	0.671746037	0.782073826	RPL13A	19q13.3
32209_at	1.39749807	1.680819295	1.459129202	1.625668474	1.791709983	FAM89B	11q23
227892_at	1.325455608	1.359556147	1.401071177	1.366002873	1.3503695	PRKAA2	1p31
201174_s_at	1.715492956	1.720103577	1.670106749	1.540121132	1.440461627	TERF2IP	16q23.1
244852_at	1.659054013	1.811744439	1.753883974	1.724030916	1.478840295	DSEL	18q22.1
213890_x_at	0.816226146	0.798662808	0.816186175	0.759957763	0.807716553	RPS16	19q13.1
200651_at	0.64542032	0.585205498	0.76129096	0.574731781	0.798937956	GNB2L1	5q35.3
226140_s_at	2.25349685	3.295001388	1.892376263	2.440956157	1.774724621	OTUD1	10p12.2
210646_x_at	0.812443671	0.765214831	0.770746116	0.708231361	0.811734326	RPL13A	19q13.3
213627_at	1.433982666	1.528351917	1.486146437	1.787823748	1.472125292	MAGED2	Xp11.2
1565681_s_at	1.286395121	1.417250601	1.613731894	1.350457736	1.489009568	DIP2C	10p15.3
223003_at	0.649578931	0.645796067	0.764290486	0.513538137	0.843146747	C19orf43	19p13.2
200716_x_at	0.773862347	0.739179966	0.748778034	0.684261902	0.7893423	RPL13A	19q13.3
201681_s_at	1.767902623	2.138774909	1.838831979	1.866502133	1.411188253	DLG5	10q23
232653_at	1.34453998	1.459573106	1.317384932	1.439607513	1.206591053	NA	NA
228598_at	1.185808989	1.216749676	1.201353376	1.201054514	1.214536238	DPP10	2q14.1
220960_x_at	0.767863868	0.786683192	0.782663468	0.753388249	0.777334007	RPL22	1p36.3-p36.2
202672_s_at	2.768877186	2.692671044	3.421454644	3.63356772	2.202649886	ATF3	1q32.3
213588_x_at	0.687687821	0.646748764	0.770644833	0.640669793	0.848144668	RPL14	3p22-p21.2
208682_s_at	1.491282502	1.606816219	1.567784066	1.868100117	1.428876904	MAGED2	Xp11.2
1556633_at	1.31549071	1.370329376	1.380701656	1.382516645	1.209629511	C1orf204	1q23.2
228601_at	1.560270915	1.647404583	1.761193119	1.674735735	1.717681684	LOC401022	2q31.2
212686_at	1.5801597	1.53841582	1.727575791	1.513558251	1.466241591	PPM1H	12q14.1-q14.2
214271_x_at	0.737449411	0.709950974	0.742482122	0.679727058	0.76487868	RPL12	9q34
201106_at	0.64320731	0.710519101	0.643171107	0.593537511	0.84334645	GPX4	19p13.3
217927_at	1.27178001	1.488356301	1.387532014	1.502109751	1.301769816	SPCS1	3p21.1
223901_at	1.27789103	1.321427088	1.295234154	1.291541971	1.417294393	SYT3	19q13.33
216873_s_at	1.293305131	1.524060428	1.443455768	1.700174818	1.599061495	ATP8B2	1q21.3
1555370_a_at	1.514808433	1.661154545	1.553448751	1.54070784	1.49175535	CAMTA1	1p36.31-p36.23
200016_x_at	0.760595138	0.711606411	0.819235232	0.71207921	0.851724877	HNRNPA1	12q13.1
231035_s_at	2.272396447	3.669171651	2.044183115	2.517617512	2.12543317	OTUD1	10p12.2
224814_at	0.439105934	0.4992916	0.543627053	0.413008225	0.552485769	DPP7	9q34.3
227796_at	0.584597795	0.520116218	0.555750895	0.472763867	0.64652925	ZFP62	5q35.3
1559826_a_at	1.793831873	2.016607132	2.269346683	1.884071357	2.041453179	LOC401074	3p12.3
221024_s_at	2.382471162	5.018119285	5.480989626	3.141043327	2.000405616	SLC2A10	20q13.1
208729_x_at	1.414322342	1.826858883	1.312173547	1.785822473	1.67468444	HLA-B	6p21.3
204065_at	1.203139091	1.374241064	1.407565353	1.274206761	1.375862632	CHST10	2q11.2
204655_at	2.518493356	2.226914354	2.211228449	1.889596411	1.446690207	CCL5	17q11.2-q12
218546_at	1.475196691	1.716234495	1.445607148	1.465866837	1.838567347	C1orf115	1q41
224570_s_at	2.059507924	2.361424107	1.644831367	2.74312296	1.428642015	IRF2BP2	1q42.3
1557410_at	1.41652687	1.500906637	1.498300014	1.280012424	1.262236638	NA	NA
1559889_at	1.482554159	1.437859509	1.637573628	1.366871432	1.291896325	NA	NA
209409_at	1.476079436	1.546298222	1.4447	1.422922605	1.479561093	GRB10	7p12-p11.2
243225_at	1.336609062	1.334458682	1.369231535	1.346489043	1.289325888	LOC283481	13q33.1
213356_x_at	0.745193958	0.722348264	0.830815098	0.723324758	0.866164964	NA	NA
216526_x_at	1.19644267	1.314181125	1.222062999	1.437254637	1.298684763	HLA-C	6p21.3
223334_at	0.569243443	0.55638359	0.676896784	0.537172557	0.714726807	TMEM126A	11q14.1
232825_s_at	1.513925951	1.633245508	1.558404819	1.536951045	1.404508496	DSEL	18q22.1
221729_at	1.322857017	1.388447747	1.294495738	1.344287623	1.326053517	COL5A2	2q14-q32
218532_s_at	1.570595194	1.573677281	1.48788005	1.510118848	1.410250911	FAM134B	5p15.1
227996_at	1.37249342	1.426133776	1.310720347	1.379717702	1.315314459	FARP1	13q32.2
211939_x_at	0.708893585	0.644506196	0.764489446	0.642389311	0.805170538	BTF3	5q13.2
200705_s_at	0.712188431	0.716355416	0.699891899	0.650873381	0.831724791	EEF1B2	2q33-q34
1559827_at	1.75928102	2.072694348	1.930408372	2.083999855	2.130520211	LOC401074	3p12.3
201406_at	0.672644365	0.634286825	0.767676575	0.655509138	0.83645124	RPL36A	Xq22.1
225525_at	1.256646042	1.321186446	1.289486438	1.289885978	1.301544849	KIAA1671	22q11.23
1555968_a_at	2.718216828	3.026299859	4.250673321	2.086848521	1.876347272	NA	NA

229782_at	3.088575868	3.251476055	2.957998752	3.157509603	3.039122848	RMST	NA
226726_at	1.368131727	1.337597945	1.332942364	1.26658765	1.292920246	MBOAT2	2p25.1
202355_s_at	0.722656539	0.70862222	0.849804025	0.668314263	0.85078957	GTF2F1	19p13.3
202052_s_at	1.503750617	1.576554209	1.483128944	1.356122794	1.503081947	RAI14	5p13.3-p13.2
229139_at	1.469630249	1.46586241	1.411722021	1.470336676	1.462306652	JPH1	8q21
214209_s_at	1.988177668	3.025119712	2.249778277	2.692747673	1.600094509	ABCB9	12q24
220201_at	0.638051348	0.534846877	0.638556462	0.473647705	0.70651857	RC3H2	9q34
212503_s_at	1.446201238	1.611207207	1.599266761	1.5236439	1.581050686	DIP2C	10p15.3
228240_at	1.306558728	1.344377955	1.309305604	1.291430795	1.582967977	NA	NA
1556794_at	1.165483915	1.217044649	1.222368498	1.185482105	1.188516274	NA	NA
201345_s_at	0.699725835	0.705259816	0.778670944	0.694866488	0.863691373	UBE2D2	5q31.2
219748_at	1.369080309	1.464205841	1.490660311	1.637543154	1.61819932	TREML2	6p21.1
1560625_s_at	1.376052362	1.5315974	1.564130414	1.582903399	1.354708269	NA	NA
218694_at	3.368755992	3.761207486	2.6274697	3.113205102	2.964779219	ARMCX1	Xq21.33-q22.2
1555759_a_at	2.060707408	1.806208607	1.865774102	1.570447846	1.356643362	CCL5	17q11.2-q12
211942_x_at	0.772846335	0.713709022	0.751529685	0.666092245	0.815445042	NA	NA
223095_at	1.47199321	1.772420998	1.479670713	1.460334948	1.292531956	MARVELD1	10q24.2
213943_at	2.118523536	2.281617217	2.151303162	2.157760179	2.218901629	TWIST1	7p21.2
233981_at	0.867372286	0.82029174	0.819085373	0.817135744	0.89746773	NA	NA
206710_s_at	1.330706783	1.327807329	1.300776506	1.272602767	1.25626959	EPB41L3	18p11.32
238155_at	1.281450325	1.356431127	1.41406435	1.155344988	1.26243193	NA	NA
200092_s_at	0.774062441	0.711509646	0.793491232	0.730220043	0.846719081	RPL37	5p13
226084_at	2.540065348	3.314544639	2.731097067	3.436854764	1.884215019	MAP1B	5q13
212233_at	2.266660341	2.836725828	2.489524323	2.964539735	1.776894401	MAP1B	5q13
218435_at	0.594952546	0.529241133	0.544640045	0.620493481	0.662375932	DNAJC15	13q14.1
208646_at	0.723675558	0.69838406	0.803110608	0.650985663	0.842610638	NA	NA
205104_at	1.219550549	1.3613506	1.404704193	1.26801731	1.259227725	SNPH	20p13
235163_at	0.787286221	0.76845991	0.669756989	0.723943726	0.800380157	MOBKL2A	19p13.3
1554980_a_at	1.900808562	2.408296434	2.376563434	2.647555999	1.862311275	ATF3	1q32.3
226026_at	0.711276421	0.752162782	0.747012551	0.72597405	0.781667466	DIRC2	3q21.1
202910_s_at	0.493088274	0.472669647	0.450400477	0.554304345	0.674191295	CD97	19p13
220484_at	1.246868277	1.250346755	1.220972067	1.195686315	1.173693539	MCOLN3	1p22.3
220606_s_at	0.732267966	0.588099563	0.652710723	0.596274964	0.797425933	C17orf48	17p13.1
208904_s_at	0.827698967	0.789386279	0.87196546	0.776648491	0.900922633	RPS28	19p13.2
212681_at	1.172630506	1.166823614	1.144623282	1.141754347	1.123964975	EPB41L3	18p11.32
208697_s_at	0.642288428	0.578829834	0.638147559	0.599488047	0.689251427	EIF3E	8q22-q23
224936_at	0.58820209	0.577211132	0.610963901	0.653085825	0.736258319	EIF2S3	Xp22.2-p22.1
202029_x_at	0.801060073	0.761818862	0.772678125	0.754601555	0.796107869	RPL38	17q23-q25
221704_s_at	1.694236915	2.016297486	1.699826159	1.93884684	1.384317975	VPS37B	12q24.31
200781_s_at	0.842054625	0.801348612	0.824460418	0.813499718	0.810637505	RPS15A	16p
229336_at	1.201993159	1.265398627	1.297730358	1.264887427	1.120864475	ST3GAL2	16q22.1
200834_s_at	0.762816752	0.777399895	0.752875603	0.749741223	0.796690655	NA	NA
200888_s_at	0.722434332	0.662737494	0.666703405	0.654076523	0.774060008	RPL23	17q
1558541_at	1.170577293	1.287374078	1.233636197	1.195455345	1.250616461	C8orf79	8p22
230326_s_at	0.730871406	0.651593367	0.749551262	0.653050057	0.748334845	C11orf73	11q14.2
226474_at	1.80784706	1.822979284	1.422744334	1.672752049	1.634476081	NLRC5	16q13
235851_s_at	1.610115213	1.984457414	1.800732043	1.583971939	1.375767741	GNAS	20q13.3
219855_at	1.69035179	1.923800727	1.663870029	1.758279968	1.778147329	NUDT11	Xp11.22
221730_at	1.249878307	1.275655077	1.291635049	1.24039089	1.206968315	COL5A2	2q14-q32
216592_at	1.691585212	2.180332704	2.424376283	1.637789854	1.866462983	MAGEC3	Xq27.2
238213_at	1.391897654	1.438233756	1.48187885	1.384451588	1.346919883	NA	NA
214434_at	1.17560529	1.244018865	1.192648974	1.223311486	1.168316065	HSPA12A	10q26.12
229899_s_at	1.790245588	2.014400229	2.103258167	1.831620525	1.607849842	C20orf199	20q13.13
213558_at	1.406872373	1.550434952	1.519718846	1.394192313	1.281727724	PCLO	7q11.23-q21.3
243428_at	1.441491967	1.669519292	1.705709813	1.299384301	1.370553439	KCNQ1OT1	11p15
208922_s_at	1.541332455	1.868837037	1.578785311	1.315917299	1.491821527	NXF1	11q12-q13
221781_s_at	1.446299206	1.936812491	1.635240916	1.338633214	1.37165577	DNAJC10	2q32.1
213227_at	1.589318455	1.965590735	1.542537365	1.357455786	1.380935013	PGRMC2	4q26
243435_at	1.388045724	1.476743815	1.399756511	1.272134274	1.307432127	KCNQ1OT1	11p15

Column 4p16 vs. D2, 4p16 vs. D1+D2, 4p16 vs. MAF, 4p16 vs. D1, 4p16 vs. 11q13 are the genes' fold changes in 4p16 subtype versus 5 other major subtypes: D2, D1+D2, MAF, D1, 11q13, respectively.

Supplemental Table 5: KEGG pathway analysis of genes associated with t(4;14).

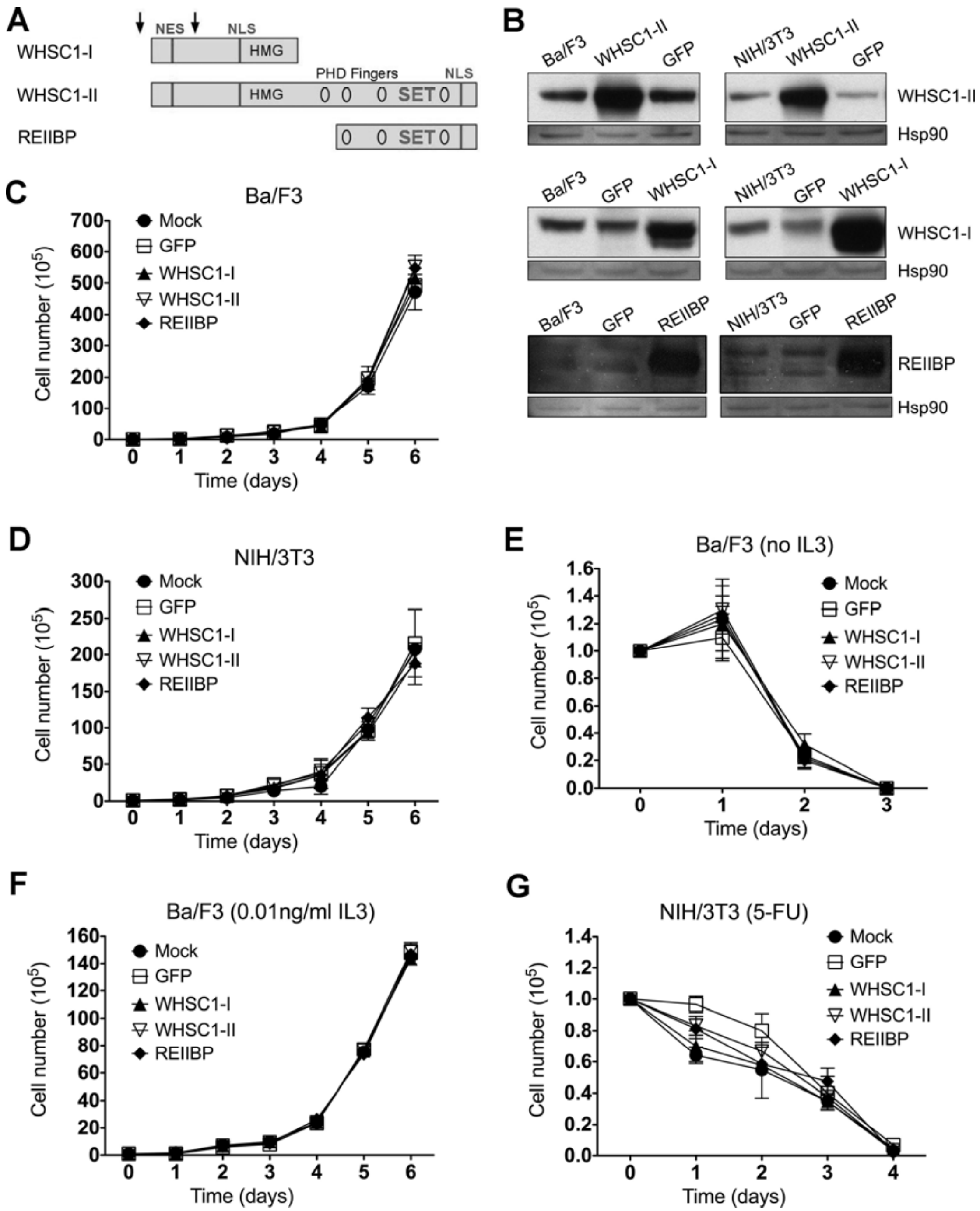
KEGGID	Term	Size	Count	ExpCount	p-value	Genes
3010	Ribosome	88	18	0.871	$4.8x10^{-20}$	RPL12, RPL21, RPL22, RPL36AL, RPL37, RPL38, RPL36A, RPS2, RPS9, RPS15, RPS15A, RPS16, RPS23, RPS25, RPS28, RPL14, RPL23, RPL13A
5416	Viral myocarditis	73	3	0.723	0.035	HLA-B, HLA-C, MYH10
4144	Endocytosis	187	5	1.85	0.036	FGFR3, HLA-B, HLA-C, VPS37B, AGAP1
4530	Tight junction	134	4	1.33	0.043	MYH10, MAGI1, EPB41L3, JAM3

Term indicates the cellular pathway identified by the Kyoto Encyclopedia of Genes and Genomes (KEGG, www.genome.jp/kegg). Count shows the number of t(4;14)-associated genes found that belong to this pathway and ExpCount is the expected count by random chance. Size is the number of all genes for the corresponding pathway. The p-value is based on the hypergeometric test of gene enrichment. Only pathways with $p<0.05$ are included.

Supplemental Table 6: Oligonucleotide primer sequences used for cloning, RT-PCR, qRT-PCR and ACA11 knock-down.

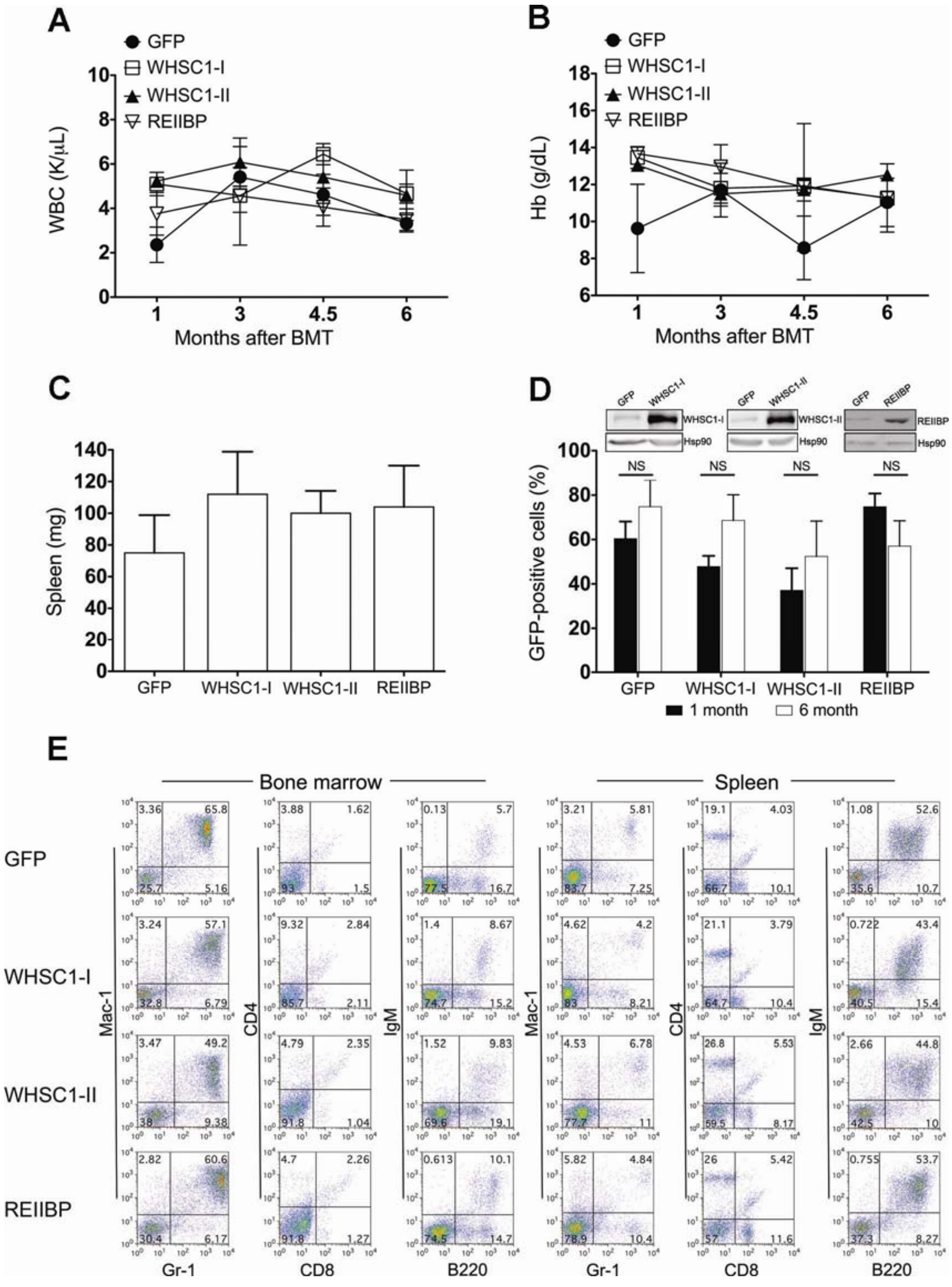
Primers used in plasmid construction	
ACA11	Fw: 5’ CCCAAGCTTGCGCTCACTAAG 3’ Rev: 5’ GCTCTAGATGTTGTACTGAAAACCG 3’
U23	Fw: 5’ CCCAAGCTTGTCTTCTCATT 3’ Rev: 5’ GCTCTAGAGAATGTCTCACA 3’
Primers used in RT-PCR and qRT-PCR assays	
ACA11	Fw: 5’ GCGCTCACTAAGGCTCGG 3’ Rev: 5’ TGTTGTACTGAAAACCG 3’
GAPDH	Fw: 5’ CTCATGACCACAGTCCATGC 3’ Rev: 5’ GGATGACCTTGCCCACAG 3’
UBC	Fw: 5’ ATTTGGGTCGCGGTTCTTG 3’ Rev: 5’ TGCCTTGACATTCTCGATGGT 3’
YWHAZ	Fw: 5’ ACTTTTGGTACATTGTGGCTTCAA 3’ Rev: 5’ CCGCCAGGACAAACCAGTAT 3’
RPL23A-1	Fw: 5’ TACGATGCTTTGGATGTTGC 3’ Rev: 5’ AAAACAAAAGGGAGCCTCGT 3’
RPL18A	Fw: 5’ AGCGGTGGTTTAAACAGAGG 3’ Rev: 5’ GTGGTGGGGAAGCGAGATAG 3’
RPL23A-2	Fw: 5’ CTGCCCCTCCTAAAGCTGA 3’ Rev: 5’ AGCGCTCTTCCGAGGATATT 3’
RPL3	Fw: 5’ AGCAAGGTTTTGACCGCTAA 3’ Rev: 5’ TGCTGATTGTCACGTTCTGA 3’ Fw: 5’-CCAAGTCATCCGTGTCATTG-3’ Rev: 5’-CCTCCGTTCACCTGGATCT-3’ Fw: 5’-ATGGAGATCCAGGTGAATGG-3’ Rev: 5’-GTTCACAGGAACCTGCTGCT-3’
RPL10	Fw: 5’ AGCCAATTAAGCCGACTGAG 3’ Rev: 5’ GGGGTAGTGCAAGGTCAGAA 3’
RPL22	Fw: 5’-GGAGCAAGAGCAAGATCACC-3’ Rev: 5’-GCGCAACCAGTCACGTAGAT-3’ Fw: 5’-TACGAGCTGCGTTACTTCCA-3’ Rev: 5’-CATTGCAGACCAATGTGTCC-3’
RPL13a	Fw: 5'-CATAGGAAGCTGGGAGCAAG-3' Rev: 5'-GCCCTCCAATCAGTCTTCTG-3' Fw: 5'-GGCTGAAGCCTACCAGAAAG-3' Rev: 5'-CTTGGCCTTTTCCTTCCGTT-3'
RPS2	Fw: 5’ CCTGCGAAAAGATGTGTGTG 3’ Rev: 5’ TCACCCGTGTGACTTTCGTA 3’ Fw: 5’-AAGATCAAGTCCCTGGAGGA-3’ Rev: 5’-AACCTCATCCTTGAGAGAGGC-3’ Fw: 5’-TGTTCTCCCTGCCCATTAAG-3’ Rev: 5’-TCTGCACTGGCATGATTTTC-3’
Sequences of ASOs	
αA1	5’ mGmUmGmGmAGAGGACCGAGmCmCmUmUmA 3’
αA2	5’ mCmAmGmUmCCTGTTTCTCTmUmGmCmUmC 3’
αA3	5’ mUmGmUmUmGTACTGAAAACmCmGmUmGmG 3’
αGFP	5’ mUmCmAmCmCTTCACCCTCTmCmCmAmCmU 3’

SUPPLEMENTAL FIGURES



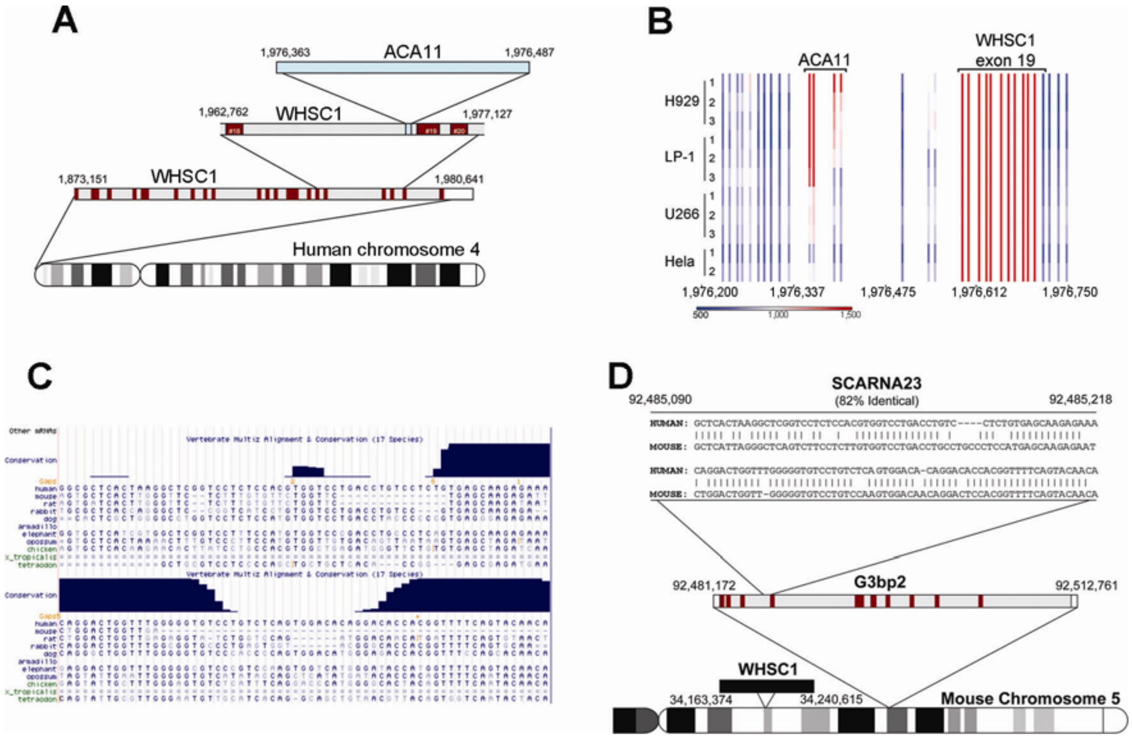
Supplemental Figure 1: Over-expression of WHSC1 proteins was not sufficient to affect cell proliferation in cell culture. (A) Cartoon of three isoforms of WHSC1. Exon 11 of WHSC1 contains poly-A/transcription stops that when included creates WHSC1-I and when skipped creates WHSC1-II. REIIBP is the result of transcription from a downstream promoter.

NLS, nuclear localization signal; NES, nucleolar exclusion signal; HMG, high mobility group domain; SET, histone methyltransferase domain; PHD, plant home domain. Arrows indicate two breakpoint cluster regions found in t(4;14)-positive patients. **(B)** Over-expression of WHSC1 protein isoforms was confirmed by Western blot analysis. Hsp90, loading control. **(C)** WHSC1 isoforms did not affect the growth of murine hematopoietic Ba/F3 cells grown in the presence of IL-3. Equal numbers (1×10^5) of stably transfected Ba/F3 cells were plated in triplicate, and the viable cells were counted by trypan blue exclusion at the indicated time points for 6 days. **(D)** Growth of stably-transfected NIH/3T3 fibroblasts was not affected by WHSC1 proteins. Cell counts were performed as described in (C). **(E** and **F)** WHSC1 proteins did not significantly affect the growth of Ba/F3 cells cultured in medium with 0 ng/ml **(E)** or 0.01 ng/ml **(F)** IL-3. Cell counts were performed as described in (C). **(G)** WHSC1 isoforms did not protect cells from cytotoxic chemotherapy. NIH/3T3 cells were cultured with 50 µg/ml 5-fluorouracil (5-FU), and cell counts were performed as described in (C). Data in **C-G** represent mean ± SD, with n=3 per group.

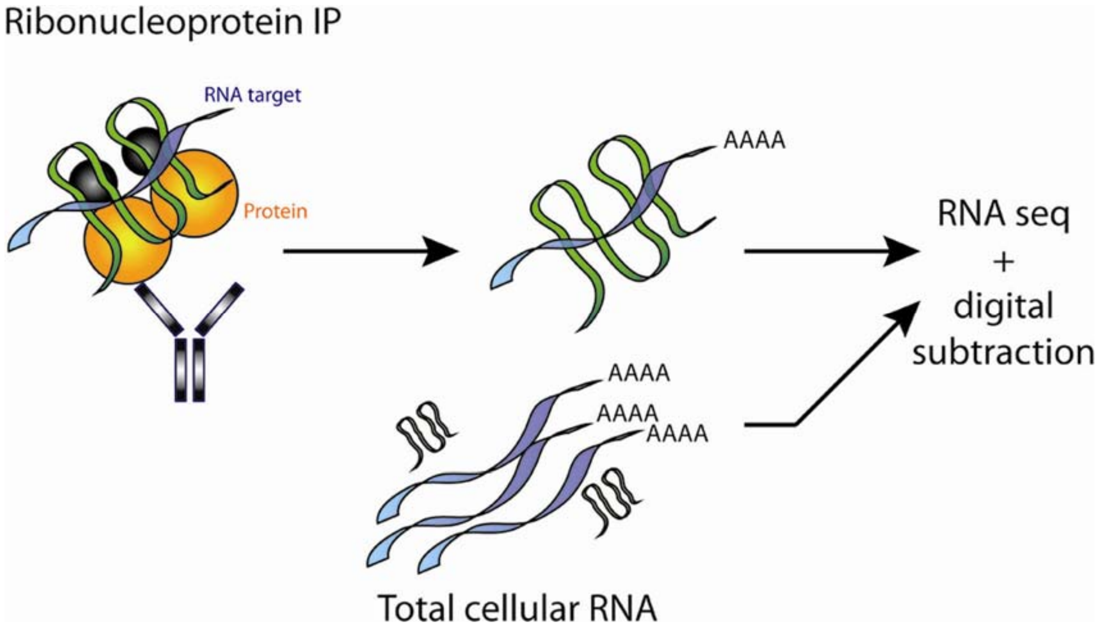


Supplemental Figure 2: WHSC1 proteins did not induce disease in tumor-prone mice. High-titer ecotropic retroviruses encoding WHSC1-I, WHSC1-II, REIIBP or GFP only control were used in bone marrow transduction-transplantation assays (BMT). Tumor-prone *Cdkn2a*$^{-/-}$

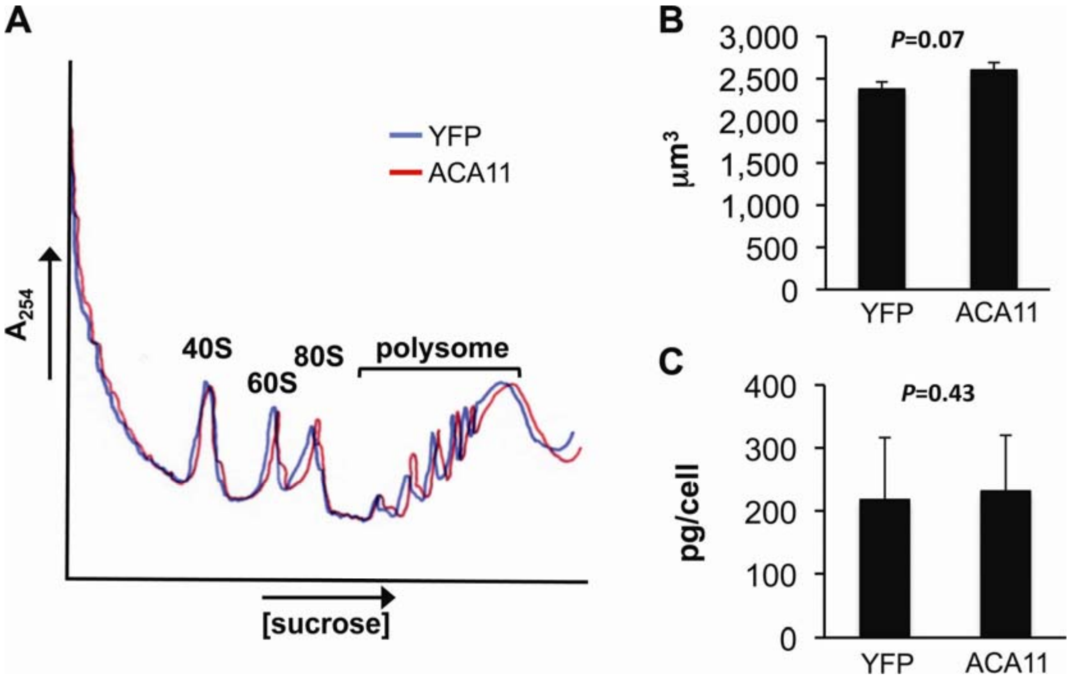
(null for both Ink4a and Arf) mice were used as bone marrow donors for all assays shown. Each group contained 5 independent transplantations. **(A)** White blood cell counts (WBC) from transplanted mice were not significantly affected by WHSC1 cDNA isoforms. **(B)** Peripheral blood hemoglobin (Hb) levels were not significantly affected by WHSC1 cDNA isoforms. **(C)** Spleen weights from WHSC1 transplanted mice sacrificed at 6 month time point showed no significant abnormality. A second set of mice transplanted with WHSC1 isoforms were followed for over one year with no consistent abnormalities found. One WHSC1-I transplanted mouse (out of 20) developed a GFP-negative leukemia. **(D)** WHSC1 cDNA isoforms did not provide significant competitive advantage to hematopoietic cells in mice. The fraction of GFP-positive peripheral blood mononuclear cells was measured at indicated time points. Over-expression of WHSC1 isoforms in the splenocytes was measured by Western blot analysis. Hsp90, loading control (inset). **(E)** Representative immunophenotype analysis of bone marrow and spleen mononuclear cells 6 months after WHSC1-isoform BMT. Cells were stained with fluorochrome-labeled antibodies as indicated. The transplanted mice demonstrated a near-normal complement of myeloid (Mac-1, Gr-1), T (CD4, CD8) and B (B220, IgM) cells. Data in **A-D** represent mean ± SD with n=5 per group. NS, non significant.



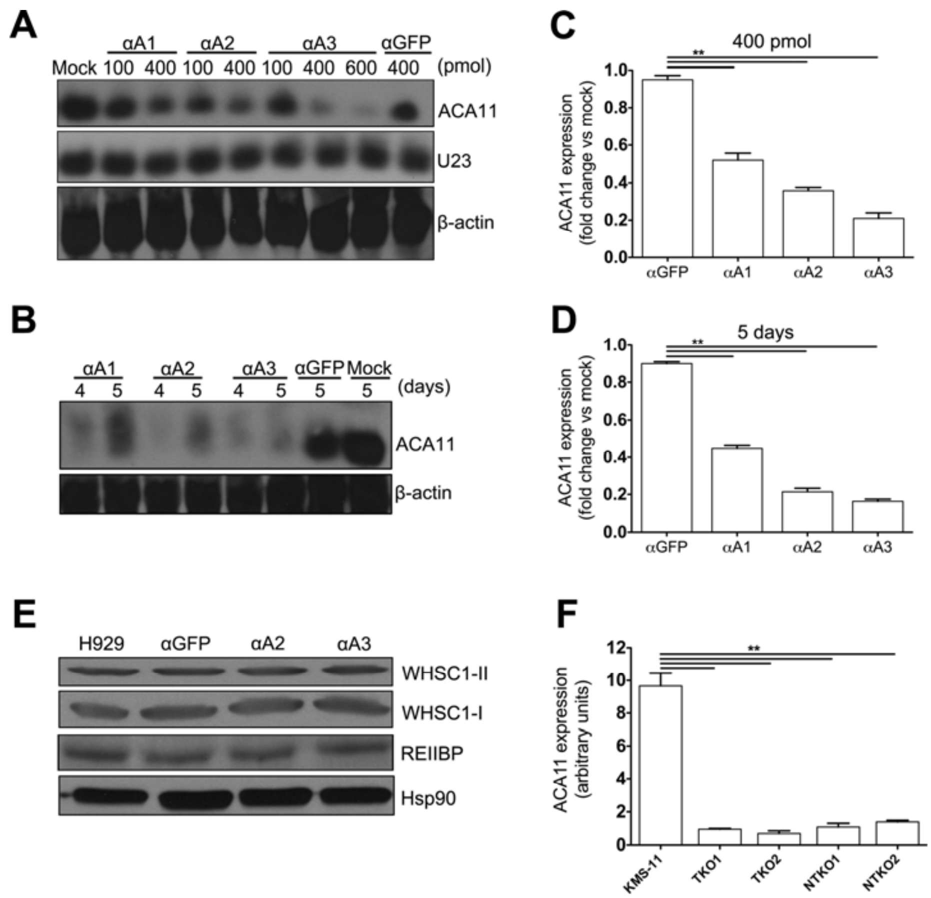
Supplemental Figure 3: ACA11 is conserved across vertebrate species, but "jumped" prior mouse evolution. (A) Schematic cartoon of ACA11's physical location on chromosome 4 within the *WHSC1* gene. **(B)** Heat map of ACA11 locus expression in cell lines analyzed by tiling arrays. Total RNAs from indicated cell lines were assayed in triplicate. The Hela cell line was tested in duplicate. **(C)** Cross-species comparison reveals only partial evolutionary conservation of the ACA11 locus. A "hole" was observed due to loss of part of the sequence in mice. **(D)** Schematic diagram of the location of the mouse version of ACA11 (SCARNA23) at a distant locus within the G3bp2 gene on chromosome 5, based on BLAST sequence similarity.



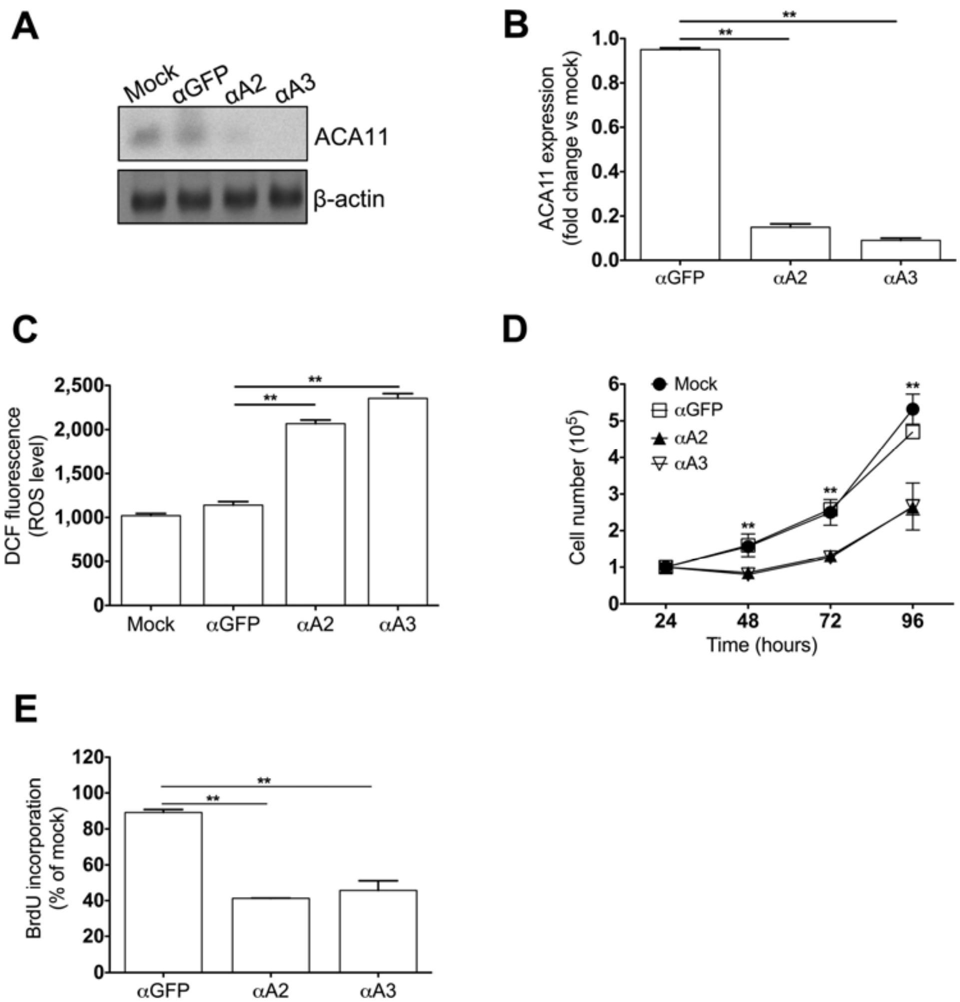
Supplemental Figure 4: Schematic diagram of deep sequencing experimental design. RNA was prepared from H929 myeloma cells using ILF3 immunoprecipitation to isolate ACA11 snRNP complex-associated RNAs. Total unfractionated RNA was isolated from H929 cells as a control. RNA libraries from each were subjected to deep sequencing and RNP-associated sequences were identified and mapped using MACS software.



Supplemental Figure 5: ACA11 did not significantly affect ribosome assembly or cell growth. (A) Polyribosome profiles were characterized in cytosolic extracts of *Arf*$^{-/-}$ MEFs over-expressing ACA11 subjected to sucrose gradients. Subtle decreases in 40S ribosomal peaks were occasionally observed in cells over-expressing ACA11, but were not consistently detected. A representative curve of 4 independent experiments showing no significant differences is shown. **(B)** Cell size measurements of *Arf*$^{-/-}$ MEFs over-expressing ACA11. **(C)** Cell mass measurements of *Arf*$^{-/-}$ MEFs over-expressing ACA11. Data in **B, C** represent mean ± SD, with n=3. P value is indicated.



Supplemental Figure 6: **Antisense oligonucleotides (ASOs) efficiently knock-down ACA11 expression without affecting WHSC1 protein expression.** **(A)** Dose-response of ASOs knock-down of ACA11 in H929 cells at 2 days after nucleofection measured by Northern blot analysis. Expression of unrelated snoRNA U23 is shown as a control. αA1, αA2 and αA3, ASOs target ACA11. αGFP, ASO targets green fluorescent protein. **(B)** Northern blot analysis of ACA11 knock-down at late time-points (4 and 5 days) following nucleofection, using 600 pmol ASO in H929 cells. **(C** and **D)** qRT-PCR expression of ACA11 in ASO knock-down H929 cells using 400 pmol ASO at 2 days after nucleofection **(C)** or 600 pmol at 5 days after nucleofection **(D)**. **(E)** Western blot analysis of WHSC1 proteins in ACA11 knock-down H929 cells using 600 pmol ASO. **(F)** ACA11 expression is severely reduced in WHSC1 knock-out KMS-11 cells (Courtesy of Ben Ho Park and Josh Lauring, Johns Hopkins University, see Lauring et al., Blood, 2008) measured by qRT-PCR. TKO, clone with knock out of the translocated *WHSC1* allele. NTKO, clone with knock out of the nontranslocated *WHSC1* allele. qRT-PCR data in **(C,D,F)** were normalized to the average of 3 reference genes (GAPDH, UBC, YWHAZ). Data are presented as mean ± SD. n=3. **$p<0.01$.



Supplemental Figure 7: Knock-down of ACA11 expression in t(4;14)-negative RPMI8226 MM cells affects oxidative stress and cell proliferation. (A) Northern blot analysis showing knock-down of ACA11 in RPMI8226 cells 96hr after nucleofection. αA2 and αA3, ASOs target ACA11. αGFP, ASO targets green fluorescent protein. **(B)** Quantification of ACA11 knock-down in RPMI8226 cells by qRT-PCR. **(C)** ROS levels measured by DCF fluorescence in ACA11 knock-down cells 48hr after nucleofection. **(D)** Reduction of cell proliferation in ACA11 knock-down cells measured by cell counting. **(E)** Reduction of BrdU incorporation in ACA11 knock-down cells 48hr after nucleofection. 600 pmol ASOs/10^6 cells were used in **(A-E).** Data in **(B-E)** represent mean ± SD, with n=3, **p<0.01.

SUPPLEMENTAL METHODS

Cell culture and transfection. NIH/3T3, 293T, A375, Hela,U1A and MEF cells were grown in Dulbecco's modified Eagle's medium (Lonza) containing 10% fetal bovine serum (FBS, Thermo), 1× penicillin-streptomycin (Pen/Strep) and 1% non-essential amino acid (Cellgro, MEF only). KMS-11, TKO, NTKO (gift of Ben Ho Park, Johns Hopkins University, Baltimore, MD), OPM-2, LP-1, RPMI8226, MM.1S, K562 and Ba/F3 cells were grown in Roswell Park Memorial Institute medium 1640 (RPMI 1640, Lonza) containing 10% FBS, 1× Pen/Strep and 1 ng/ml recombinant mouse interleukin-3 (R&D, Ba/F3 only). U266 and H929 cells were grown in RPMI 1640 (ATCC) containing 10% FBS, 1× Pen/Strep and 0.05 mM 2-mercaptoethanol (Sigma, H929 only). Primary murine bone marrow mononuclear cells were grown in transplant medium consisting of RPMI 1640 (Lonza), 20% FBS, 1× Pen/Strep, 10 ng/ml stem cell factor (SCF, R&D), 6 ng/ml IL-3, 50 ng/ml Flt-3 (R&D), and 10 ng/ml thrombopoietin (PeproTech). Cells were maintained at 37°C in a 5% CO_2 humidified incubator. Cells were transfected using polyfect transfection reagent (QIAGEN) according to the manufacturer's protocol. We used MEFs null for the ribosome biogenesis regulator Arf ($Arf^{-/-}$).

Plasmid constructs. Amplification of the coding region of human ACA11 or U23 was performed according to the protocol of REDExtract-N-Amp tissue PCR kit (Sigma). Primer sequences are listed in **Supplemental Table 6.** The amplified DNA was subcloned to HindIII/XbaI-linearized pBluescript II KS (+) vector (Stratagene) (pBS-ACA11). Lentiviral vector FCY-si was provided by Jeff Milbrandt (Washington University in St. Louis). It contains a U6 promoter upstream from the cloning site and expresses the yellow fluorescent protein (YFP). The 125bp ACA11 oligonucleotides were annealed and ligated into AgeI/BamHI-linearized FCY-si vector. The expression vector pEGFP-C1-NPM1 was provided by Jason Weber (Washington University in St. Louis). The cDNAs encoding human WHSC1-I, WHSC1-II or REIIBP (provided by Pierre-Olivier Angrand, Cellzome AG, Heidelberg, Germany) were subcloned to the retroviral vector MSCV-IRES-GFP (provided by Warren Pear, University of Pennsylvania). The identity of all constructs was verified by sequencing analysis.

Virus production. Recombinant lentivirus or retrovirus was generated by transient cotransfection of 293T cells with lentiviral or retroviral transducing vector, and packaging vectors pMD.G and pCMVdeltaR8.91 (for lentivirus) or pMD.G and pMD-gagpol (for amphotropic retrovirus) or Ecopac (for ecotropic retrovirus). Viral supernatant was harvested 48 hours after transfection, and the titer of the infectious virus was determined by measuring percentage of YFP- or GFP-positive cells using NIH/3T3 cells infected with serial dilutions of virus in the presence of 10 μg/ml of polybrene (American Bioanalytical). The stable transduced cells were obtained by sorting based on equivalent GFP or YFP expression levels.

Murine bone marrow transduction-transplantation (mBMT) and mice phenotype analysis. Mice (Jackson) were maintained in the animal facility at Washington University in St. Louis according to proper institutional guidelines. Retroviral transduction and transplantation of bone marrow cells were performed as described (1). *Cdkn2a*$^{-/-}$ (exon 2 knockouts null for both Ink4a and Arf proteins) mice were used as bone marrow donors. Peripheral blood was obtained by retroorbital phlebotomy and blood counts were analyzed (Hemavet, CDC technologies). Spleen and liver weight were recorded when mice were sacrificed.

Flow cytometry. Flow cytometry was performed as described (2). Antibodies used in the current analysis were anti-CD4, anti-CD8, anti-Mac-1, anti-Gr-1, anti-IgM and anti-B220 (BD). Acquisition was performed on the CellQuest software (BD) and data analysis was performed on the FLOWJO software (Tree Star).

Cell fractionation. Cells were swollen in a hypotonic buffer (10 mM HEPES-KOH pH 7.9, 1.5 mM $MgCl_2$, 10 mM KCl, 0.5 mM DTT) for 30 min and homogenized with a Kontes Dounce homogenizer. The dounced cells were centrifuged at 1200rpm for 5 min, and the supernatant was retained as the cytoplasmic fraction. The nuclear pellet was resuspended in 450 µl of 0.25 M sucrose/10 mM $MgCl_2$ and layered over equal volume of 0.35 M sucrose/0.5 mM $MgCl_2$, then centrifuged at 3000rpm for 5 min. The clean, pelleted nuclei were resuspended in 750 µl of 0.35 M sucrose/0.5 mM $MgCl_2$ and sonicated for 8X10 sec (with 30 sec rest between each sonication) with a sonic dismembrator (Thermo) until all the nuclei were disrupted. The sonicated samples were layered over equal volume of 0.88 M sucrose/0.5 mM $MgCl_2$ and centrifuged at 2800g for 10 min in a horizontal rotor. The upper layers, constituting the nucleoplasmic fraction, were carefully removed. The nucleolar pellets were washed by resuspending in 500 µl of 0.35 M sucrose/0.5 mM $MgCl_2$ and centrifuged at 2800g for 10 min. All steps were carried out at 4°C. Each preparation was controlled under the phase-contrast microscope.

RNA electrophoretic mobility shift assay. The plasmid pBS-ACA11 was linearized with XbaI and incubated with T3 RNA polymerase. The 3' end biotinylated ACA11 RNA was generated using T4 RNA ligase (Pierce). 5 ng of RNA was incubated with 0.5 µg of native nuclear protein extracts (prepared using NE-PER nuclear and cytoplasmic extraction reagents, Pierce), and the EMSA binding buffer (10 mM HEPES pH7.3, 20 mM KCl, 1 mM $MgCl_2$, 1 mM DTT), 5% glycerol, 10 µg tRNA for 25 min at room temperature. Complexes were resolved by 6% nondenaturing polyacrylamide gel (0.5 x Tris borate-EDTA, pH8.3) for 3 hr at 10V/cm and transferred to a nylon membrane (Thermo) at 400 mA for 30 min and fixed by UV cross-linking. Blocking and detection of biotin-labeled bands was performed using the LightShift Chemiluminescent RNA EMSA kit (Thermo) according to the manufacturer's instructions. Experiments were repeated 3 times.

RNA affinity chromatography. 10 μg of biotinylated ACA11 RNA was incubated with 150 μg of native nuclear extracts in the EMSA binding buffer for 25 min at room temperature. The mixture was further incubated with 100 μl of high capacity streptavidin agarose resin (Pierce) for 2 hr at 4°C with rotation. Reaction without the addition of biotinylated RNA served as negative control. The resins were centrifuged for 2 min at 3000g and washed six times with the binding buffer. The resins were boiled for 5 min in loading buffer to release captured proteins, which were resolved on an 8% SDS-PAGE gel. The proteins were commassie-stained with the GelCode blue stain reagent (Pierce) and those prominently captured bands were excised for mass spectrometry analysis.

RNA sequencing. The whole transcriptome libraries were generated according to IIlumina protocol. Briefly, the RNA fragments were ligated to RNA 3' adapter and 5' adapter using T4 RNA ligase. The equivalent of adapter-ligated RNAs were then incubated with the SRA RT primer at 65°C for 10 min. Reverse transcription was performed by incubating the mixture for 1 hr at 44°C with the SuperScript III reverse transcriptase (Invitrogen). The reverse transcribed cDNAs were amplified by a 12 cycles of PCR with small RNA PCR primer 1.0 and small RNA PCR primer 2.0, ensured on a PAGE gel, and purified by using the Agencourt AMPure XP beads (Beckman Coulter). The libraries were validated by using the Agilent Technologies 2100 bioanalyzer and submitted for sequencing on the Illumina HiSeq 2000 platform. The MACS (Model-based Analysis for ChIP-Seq) algorithm was used to discover regions enhanced in the pull-down sample compared to the total input control RNA sample. The peaks called by MACS were sorted by number of tags to give the top fifty enhanced RNAs. Data were imported into and visualized in USCS Genome Browser. Experiments were repeated 2 times.

SnoRNA knock-down. The antisense oligonucleotides (ASOs) were designed as complementary sequences to ACA11. ASOs were 20-nucleotides (nt) long and comprised 10 deoxyribonucleotides flanked by 5nt 2'-O-methyloxylethyl (2'-O-MOE) modified ribonucleotides at both sides. All ASOs were covered by phosphorothioate (IDT). Cells were resuspended in 100 μl of solution V (Cell Line Nucleofector Kit V, Amaxa) and mixed with the ASOs. Transfection was carried out using program T-001 (H929), G015 (RPMI8226) or O-10 (KMS-11) on the Amaxa nucleofector instrument. Cells were subsequently cultured in complete growth medium for further analysis. The sequences of ASOs are listed in **Supplemental Table 6.**

Ribosome fractionation. Ribosome profiles were performed as described previously (25). Briefly, cells were treated with 10 μg/ml cycloheximide prior to harvesting and counting. Cytosolic extracts from equal numbers of cells ($3x10^6$) were separated over sucrose gradients. The gradients were fractionated with an ISCO Teledyne Gradient Fractionator with constant absorbance monitored at 254nm. Experiments were repeated 4 times.

Xenograft mouse model. 6-week-old male triple immune-deficient BNX mice were obtained from NCI-Frederick and maintained in an accredited animal facility according to proper institutional guidelines. Cells were nucleofected with ACA11 ASOs, incubated at 37°C for 48 hr, washed twice and mixed with same volume of matrigel basement membrane matrix (BD). $8.5x10^6$ mock or knock-down cells were subcutaneously injected into the right flank of each mouse. Tumors were constantly monitored and the tumors' volume was calculated using the formula: $4/3 \times (width/2)^2 \times (length/2)$.

Antibodies. Antibodies to WHSC1-I, WHSC1-II, Hsp90, NCL, Lamin B, RPL22, RPL3, RPS2, γ-tubulin, IgG (Santa Cruz), Drosha, DHX9, ADAR, ILF3, PARP1 (Abcam), DNA-PK, RPL13a

(Cell Signaling), SF3B1, hnRNP U (Novus), DDX21, DDX5 (Bethyl), SOD (Cal Biochem), NUP62 (Covance), NPM1 (Invitrogen) and REIIBP (made by our lab) were used as primary antibodies for western blot or immunoprecipitation. Blots were incubated with horseradish peroxidase-conjugated secondary antibodies (Amersham Biosciences) and visualized by enhanced chemiluminescence (Pierce Biotechnology). Images were analyzed using Image Lab 3.0 software (Bio-Rad). Experiments were repeated 3 times.

SUPPLEMENTAL REFERENCES

1. Tomasson MH, et al. Fatal myeloproliferation, induced in mice by TEL/PDGFbetaR expression, depends on PDGFbetaR tyrosines 579/581. *J Clin Invest.* 2000; 105 (4): 423-432.

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