

## Supplementary Materials for

### **A somatic mutation in moesin drives progression into acute myeloid leukemia**

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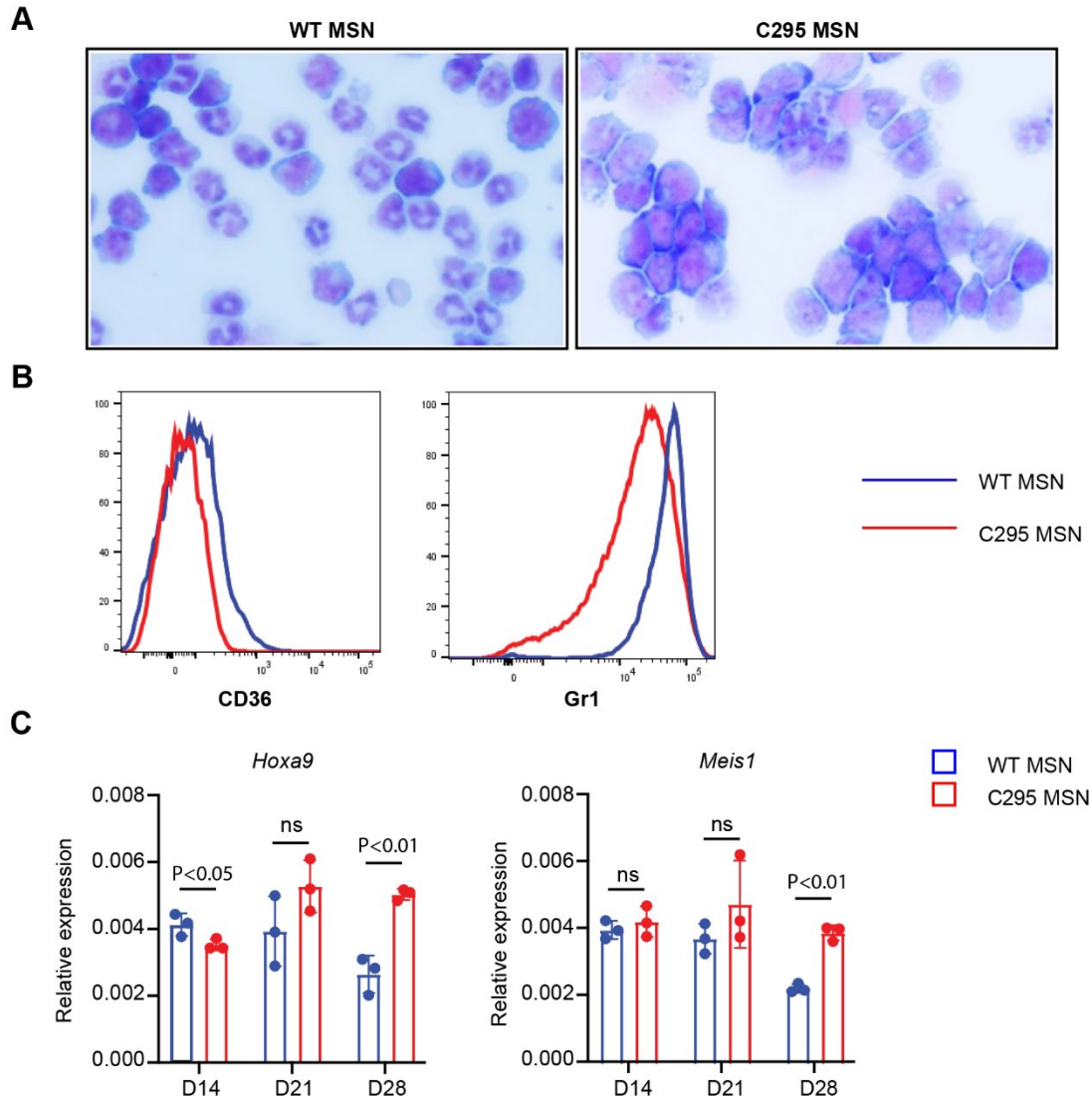
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Figs. S1 and S2  
Tables S1 to S4

			pGM_2_4	pGM_2_6	pGM_3_8	pGM_3_9	pGM_3_10	pGM_3_11	pGM_3_12	pGM_4_13	pGM_4_15	CLP_3	GML_P_2	GML_P_3	pGM_1_3	pGM_1_2	pGM_2_5	pGM_4_16	CLP_2	pGM_3_7	GML_P_1	pGM_1_1	
Ras signaling pathway	Msn*																						
	Ptpn11*	(6,10,11,31)																					
	Hras	(6,10,12,31)																					
	Braf	(6,12)																					
PI3K-Akt signaling pathway	Gnb2	(8)																					
	Reln	(21)																					
Adhesion and Migration	Adam29	(22)																					
	Fat1	(23)																					
	Fat4	(23)																					
Transcription	Setbp1	(31)																					
JAK-STAT signaling	Epor	(24)																					
Chromatin modification	Smarcad1	(25)																					
	Kdm6a	(6)																					
RTK signaling pathway	Csflr	(26)																					
Cell cycle	Ccnd3	(31)																					
	Cdk4*	(20)																					
G-protein receptor or Tumor suppression	Sipa112	(27)																					
Other	Robo2	(28)																					
	Spata16	(29)																					
	Ryr1	(30)																					
	Cdh11*																						
	Fbxo22*																						
	Sh2d1b1*																						
	Exo1*																						

**Fig. S1. Distribution of recurrently mutated genes from our study.** Each column indicates individual AML samples from our work. Asterisks mark recurrent mutations in our study. Dark gray boxes denote mutations with AF higher than 0.3 and light gray boxes denote mutations with AF higher than 0.1 but lower than 0.3. References (column 3) refer to previous studies where the gene has been found mutated in AML.



**Fig. S2. C295 MSN inhibits differentiation of leukemia-propagating AML cells (connected to Figure 3).** (A) Representative cytopspins following May–Grünwald–Giemsa staining of GFP+ MLL-ENL expressing BM cells transduced with WT (left) or C295 mutant MSN (right) at 28 days after transplantation. (B) Representative FACS analysis for differentiation markers CD36 and Gr1 on GFP+ MLL-ENL expressing BM cells transduced with WT or C295 mutant MSN at 28 days after transplantation. (C) mRNA expression of *Hoxa9* and *Meis1* in GFP+ MLL-ENL in LIC with WT or C295 mutant MSN at different time points after transplantation. Data show mean  $\pm$  SD from three biological replicates (individual mice) per time point.

**Table S1.**

**Somatic mutations identified in leukemic samples by WGS/WES (n=25).**

Table S1 (CLP, GMLP, pGM_1)																			
Sample ID	INPUT	PROTEIN_ID	LENGTH	STRAND	CODON_CHANGE	POS	RESIDUE_REF	RESIDUE_ALT	TYPE	PROVEAN SCORE	PROVEAN PREDICTION (cutoff=-2.5)	#SEQ for PROVEAN PREDICTION	#CLUSTER for PROVEAN PREDICTION	SIFT SCORE	SIFT PREDICTION (cutoff=0.05)	SIFT_MEDIAN_INFO	#SEQ for SIFT PREDICTION	GENE_NAME	VAF
CLP_1	19,70966 25,G,A,0 .515	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	186	R	W	Single AA Change	-4.35	Deleterious	242	30	0.001	Damaging	2.93	123	Flrt1	0.515
CLP_1	15,79717 661,G,A, 0.475	ENSMU SP00000 043575	668	1	ACA G[G/A] A GAC	535	G	E	Single AA Change	-7.5	Deleterious	109	30	0.001	Damaging	2.85	182	Gtpbp1	0.475
CLP_1	8,932718 86,C,T,0. 522	ENSMU SP00000 034178	561	-1	TAC [G/A]A A AAT	161	E	K	Single AA Change	-3.51	Deleterious	205	30	0.001	Damaging	2.79	320	Ces1f	0.522
CLP_1	9,423454 70,G,A,0 .109	ENSMU SP00000 040262	2155	-1	TTG [C/T]G G GGG	1637	R	W	Single AA Change	-3.47	Deleterious	84	30	0.025	Damaging	2.87	68	Tecta	0.109
CLP_1	7,120940 331,C,T, 0.476	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	460	R	W	Single AA Change	-4.12	Deleterious	132	30	0.002	Damaging	3.17	92	Polr3e	0.476
CLP_3	19,70966 25,G,A,0 .484	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	186	R	W	Single AA Change	-4.35	Deleterious	242	30	0.001	Damaging	2.93	123	Flrt1	0.484
CLP_3	6,432363 57,T,C,0. 404	ENSMU SP00000 077204	321	1	CTC [T/C]T C TTT	250	F	L	Single AA Change	-5.36	Deleterious	532	30	0.01	Damaging	2.82	394	Olf47	0.404
CLP_3	8,102673 895,A,T, 0.113	ENSMU SP00000 074681	796	-1	ATT G[T/A] T AAG	147	V	D	Single AA Change	-5.77	Deleterious	442	30	0	Damaging	3.04	391	Cdh11	0.113
CLP_3	9,552211 51,G,T,0 .146	ENSMU SP00000 034859	402	1	GGA G[G/T] C CAG	252	G	V	Single AA Change	-4.33	Deleterious	72	30	0.003	Damaging	2.87	45	Fbxo22	0.146

CLP_3	5,121143 098,A,G, 0.122	ENSMU SP00000 058757	597	-1	AGG [T/C]C G GGG	50 6	S	P	Single AA Change	-4.51	Deleteriou s	180	30	0.03 9	Damagi ng	2.85	194	Ptpn11	0.122
CLP_3	7,120940 331,C,T, 0.538	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleteriou s	132	30	0.00 2	Damagi ng	3.17	92	Polr3e	0.538
CLP_3	X,93777 402,C,A, 0.250	ENSMU SP00000 036604	415	-1	GGC TT[G/T ]CCA	32 8	L	F	Single AA Change	-3.81	Deleteriou s	281	30	0.00 1	Damagi ng	2.78	303	Pdk3	0.25
CLP_5	5,109086 487,A,T, 0.449	ENSMU SP00000 093612	831	-1	AGC [T/A]A C ATC	62 0	Y	N	Single AA Change	-8.28	Deleteriou s	247	30	0.00 3	Damagi ng	2.78	312	Vmn2r12	0.449
CLP_5	19,70966 25,G,A,0 .533	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleteriou s	242	30	0.00 1	Damagi ng	2.93	123	Flrt1	0.533
CLP_5	5,109174 184,CT, AC,0.21 4	ENSMU SP00000 052977	831	-1	GAC CA[AG /GT]GT ATT	21 6	G	C	Single AA Change	-7.38	Deleteriou s	271	30	0.00 5	Damagi ng	2.73	341	Vmn2r13	0.214
CLP_5	16,73933 720,T,A, 0.552	ENSMU SP00000 112285	118 8	-1	ACA CA[A/ T] ATC	10 05	Q	H	Single AA Change	-2.94	Deleteriou s	173	30	0.00 4	Damagi ng	2.99	156	Robo2	0.552
CLP_5	7,120940 331,C,T, 0.419	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleteriou s	132	30	0.00 2	Damagi ng	3.17	92	Polr3e	0.419
CLP_5	3,891503 70,G,C,0 .220	ENSMU SP00000 029686	779	-1	CTG AG[C/ G] GAG	40 6	S	R	Single AA Change	-2.79	Deleteriou s	199	30	0.00 1	Damagi ng	2.83	250	Hcn3	0.22
CLP_5	8,102674 037,T,A, 0.154	ENSMU SP00000 074681	796	-1	ACC [A/T]T T TTT	10 0	I	F	Single AA Change	-2.99	Deleteriou s	442	30	0.02 5	Damagi ng	3.07	389	Cdh11	0.154
CLP_5	1,550786 48,C,T,0. 162	ENSMU SP00000 027123	573	-1	GCA [G/A]G T GTT	48 4	G	S	Single AA Change	-5.08	Deleteriou s	270	30	0.00 1	Damagi ng	3.15	383	Hspd1	0.162
CLP_5	X,96160 175,C,T, 0.970	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleteriou s	266	30	0	Damagi ng	2.89	331	Msn	0.97
GMLP_1	19,70966 25,G,A,0 .471	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleteriou s	242	30	0.00 1	Damagi ng	2.93	123	Flrt1	0.471
GMLP_1	5,145123 679,C,T, 0.114	ENSMU SP00000 082822	372	1	CTC [C/T]G G ATC	94	R	W	Single AA Change	-7.21	Deleteriou s	161	30	0	Damagi ng	2.87	182	Arpc1b	0.114

GMLP_1	7,120940 331,C,T, 0.488	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.488
GMLP_1	5,309169 76,T,G,0 .290	ENSMU SP00000 031055	101 7	1	CAG G[T/G] G AAG	18 7	V	G	Single AA Change	-5.16	Deleterious	121	30	0.00 1	Damaging	2.82	43	Emilin1	0.29
GMLP_5	19,70966 25,G,A,0 .500	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleterious	242	30	0.00 1	Damaging	2.93	123	Flrt1	0.5
GMLP_5	11,77441 923,T,A, 0.354	ENSMU SP00000 042625	142 3	1	GTG A[T/A] T GCC	40 4	I	N	Single AA Change	-6.92	Deleterious	113	30	0	Damaging	3.17	370	Ssh2	0.354
GMLP_5	11,97711 239,A,C, 0.121	ENSMU SP00000 099436	205	1	GAA C[A/C] A ATG	14 5	Q	P	Single AA Change	-4.46	Deleterious	267	30	0.03 4	Damaging	2.78	366	Psmb3	0.121
GMLP_5	11,97711 247,G,A, 0.113	ENSMU SP00000 099436	205	1	TAT [G/A]G G ATG	14 8	G	R	Single AA Change	-7.79	Deleterious	267	30	0.01 2	Damaging	2.78	366	Psmb3	0.113
GMLP_5	7,120940 331,C,T, 0.486	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.486
GMLP_5	8,102674 078,C,A, 0.286	ENSMU SP00000 074681	796	-1	GAT G[G/T] G AAC	86	G	V	Single AA Change	-7.53	Deleterious	442	30	0	Damaging	3.06	387	Cdh11	0.286
GMLP_5	X,98286 643,G,A, 0.750	ENSMU SP00000 052648	899	1	TTT C[G/A] G AGG	58 7	R	Q	Single AA Change	-3.23	Deleterious	210	30	0.00 4	Damaging	3.09	302	Ar	0.75
GMLP_5	X,96160 175,C,T, 0.900	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.9
GMLP_6	19,70966 25,G,A,0 .538	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleterious	242	30	0.00 1	Damaging	2.93	123	Flrt1	0.538
GMLP_6	16,81615 718,G,A, 0.220	ENSMU SP00000 063468	837	1	AAT G[G/A] C CTT	69 8	G	D	Single AA Change	-3.09	Deleterious	200	30	0.00 2	Damaging	2.94	142	Ncam2	0.22
GMLP_6	11,97711 239,A,C, 0.120	ENSMU SP00000 099436	205	1	GAA C[A/C] A ATG	14 5	Q	P	Single AA Change	-4.46	Deleterious	267	30	0.03 4	Damaging	2.78	366	Psmb3	0.12
GMLP_6	11,97711 247,G,A, 0.106	ENSMU SP00000 099436	205	1	TAT [G/A]G G ATG	14 8	G	R	Single AA Change	-7.79	Deleterious	267	30	0.01 2	Damaging	2.78	366	Psmb3	0.106

GMLP_6	9,552211 51,G,T,0 .149	ENSMU SP00000 034859	402	1	GGA G[G/T] C CAG	25 2	G	V	Single AA Change	-4.33	Deleterious	72	30	0.00 3	Damaging	2.87	45	Fbxo22	0.149
GMLP_6	7,290549 29,T,C,0. 128	ENSMU SP00000 032813	503 3	-1	ACC G[A/G] C CAG	35 28	D	G	Single AA Change	-6.16	Deleterious	146	30	0.00 1	Damaging	2.85	202	Ryr1	0.128
GMLP_6	7,120940 331,C,T, 0.400	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.4
GMLP_6	7,126996 317,A,C, 0.278	ENSMU SP00000 127250	870	-1	CTG G[T/G] C CGA	20 7	V	G	Single AA Change	-6.15	Deleterious	101	30	0.00 1	Damaging	2.78	97	Mvp	0.278
GMLP_6	1,163257 816,G,A, 0.114	ENSMU SP00000 027878	245	-1	CCT [C/T]G T CCT	18 2	R	C	Single AA Change	-4.82	Deleterious	116	30	0.01 3	Damaging	2.83	90	Prrx1	0.114
GMLP_6	19,58730 589,G,T, 0.125	ENSMU SP00000 045465	473	1	GTT [G/T]A C ATG	10 7	D	Y	Single AA Change	-6.85	Deleterious	151	30	0.00 1	Damaging	2.83	165	Pnlipr1	0.125
GMLP_6	7,102909 257,C,G, 0.243	ENSMU SP00000 062385	322	-1	GCT C[G/C] C CTA	19 4	R	P	Single AA Change	-4.43	Deleterious	706	30	0.00 1	Damaging	2.8	354	Olfir571	0.243
GMLP_6	X,96160 175,C,T, 0.500	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.5
pGM_1	19,70966 25,G,A,0 .570	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleterious	242	30	0.00 1	Damaging	2.93	123	Flrt1	0.57
pGM_1	18,61118 997,T,A, 0.469	ENSMU SP00000 025523	977	1	GTG G[T/A] G GTG	51 7	V	E	Single AA Change	-3.76	Deleterious	201	30	0.00 1	Damaging	2.79	78	Csflr	0.469
pGM_1	1,170277 442,G,A, 0.101	ENSMU SP00000 137069	132	1	GGA [G/A]G T GTG	23	G	S	Single AA Change	-4.07	Deleterious	85	30	0.03 9	Damaging	2.76	42	Sh2d1b1	0.101
pGM_1	2,152687 626,C,T, 0.275	ENSMU SP00000 100534	181	1	TCT C[C/T] T GGA	11 9	P	L	Single AA Change	-7.94	Deleterious	158	30	0.00 8	Damaging	2.86	190	Mcts2	0.275
pGM_1	9,389757 69,T,C,0. 544	ENSMU SP00000 075102	308	1	CTG T[T/C] C CTG	31	F	S	Single AA Change	-6.82	Deleterious	473	30	0	Damaging	3.27	398	Olfir933	0.544
pGM_1	9,552211 51,G,T,0 .262	ENSMU SP00000 034859	402	1	GGA G[G/T] C CAG	25 2	G	V	Single AA Change	-4.33	Deleterious	72	30	0.00 3	Damaging	2.87	45	Fbxo22	0.262

pGM_1	7,120940 331,C,T, 0.622	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.622
pGM_1	4,124707 326,C,A, 0.108	ENSMU SP00000 040150	289	1	CAG [C/A] G CTG	13 5	P	Q	Single AA Change	-6.06	Deleterious	209	30	0	Damaging	2.9	225	Fhl3	0.108
pGM_1	10,12706 4302,G, A,0.343	ENSMU SP00000 006911	303	1	AAA [G/A]C C CGA	23	A	T	Single AA Change	-3.54	Deleterious	145	30	0.00 6	Damaging	2.88	199	Cdk4	0.343
pGM_1	7,289772 24,T,G,0 .256	ENSMU SP00000 066038	218	-1	GAG [A/C]C C TGC	11 1	T	P	Single AA Change	-3.09	Deleterious	124	30	0.03 7	Damaging	2.83	115	Eif3k	0.256
pGM_1	1,175886 763,G,A, 0.364	ENSMU SP00000 039376	837	1	GAC [G/A]G A TGT	79	G	R	Single AA Change	-7.12	Deleterious	82	30	0	Damaging	2.86	93	Exo1	0.364
pGM_5	19,70966 25,G,A,0 .490	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleterious	242	30	0.00 1	Damaging	2.93	123	Flrt1	0.49
pGM_5	9,383784 15,A,G,0 .186	ENSMU SP00000 072514	316	1	TCT [A/A]G C ATC	17 8	N	S	Single AA Change	-4.09	Deleterious	572	30	0.02 8	Damaging	3.35	398	Olfir251	0.186
pGM_5	2,152687 626,C,T, 0.402	ENSMU SP00000 100534	181	1	TCT [C/T] T GGA	11 9	P	L	Single AA Change	-7.94	Deleterious	158	30	0.00 8	Damaging	2.86	190	Mcts2	0.402
pGM_5	X,96160 175,C,T, 0.260	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.26
pGM_5	10,12706 4302,G, A,0.145	ENSMU SP00000 006911	303	1	AAA [G/A]C C CGA	23	A	T	Single AA Change	-3.54	Deleterious	145	30	0.00 6	Damaging	2.88	199	Cdk4	0.145
pGM_5	7,120940 331,C,T, 0.405	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.405
pGM_5	7,305678 99,T,C,0 .171	ENSMU SP00000 042312	345	1	AAA [T/C] T GGC	34 4	L	P	Single AA Change	-5.92	Deleterious	29	13	0	Damaging	2.82	27	Igflr1	0.171
pGM_5	1,175886 763,G,A, 0.200	ENSMU SP00000 039376	837	1	GAC [G/A]G A TGT	79	G	R	Single AA Change	-7.12	Deleterious	82	30	0	Damaging	2.86	93	Exo1	0.2
pGM_5	17,24408 242,C,G, 0.243	ENSMU SP00000 045285	170 4	1	GCC [C/G]G A GAG	15 61	R	G	Single AA Change	-5.45	Deleterious	86	30	0.04 2	Damaging	2.8	82	Abca3	0.243



pGM_5	6,245643 12,A,T,0 .200	ENSMU SP00000 031696	583	1	GGA A[A/T] C CCT	25 5	N	I	Single AA Change	-6.34	Deleterious	162	30	0	Damaging	2.78	129	Asb15	0.2
pGM_5	15,10148 8420,T, G,0.231	ENSMU SP00000 023718	479	-1	GAA GA[A/ C] GTT	19 5	E	D	Single AA Change	-2.73	Deleterious	414	30	0.00 1	Damaging	3.2	397	5430421 N21Rik	0.231
pGM_7	19,70966 25,G,A,0 .495	ENSMU SP00000 109010	674	-1	AGC [C/T]G G AAC	18 6	R	W	Single AA Change	-4.35	Deleterious	242	30	0.00 1	Damaging	2.93	123	Flrt1	0.495
pGM_7	1,170277 442,G,A, 0.125	ENSMU SP00000 137069	132	1	GGA [G/A]G T GTG	23	G	S	Single AA Change	-4.07	Deleterious	85	30	0.03 9	Damaging	2.76	42	Sh2d1b1	0.125
pGM_7	2,152687 626,C,T, 0.386	ENSMU SP00000 100534	181	1	TCT C[C/T] T GGA	11 9	P	L	Single AA Change	-7.94	Deleterious	158	30	0.00 8	Damaging	2.86	190	Mcts2	0.386
pGM_7	11,97711 239,A,C, 0.101	ENSMU SP00000 099436	205	1	GAA C[A/C] A ATG	14 5	Q	P	Single AA Change	-4.46	Deleterious	267	30	0.03 4	Damaging	2.78	366	Psm3	0.101
pGM_7	5,136991 608,A,T, 0.114	ENSMU SP00000 004968	741	1	TAT G[A/T] C ACA	52 5	D	V	Single AA Change	-4.24	Deleterious	183	30	0.01 3	Damaging	2.88	194	Plod3	0.114
pGM_7	X,96160 175,C,T, 0.545	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.545
pGM_7	7,120940 331,C,T, 0.538	ENSMU SP00000 033173	710	1	CAG [C/T]G G GTC	46 0	R	W	Single AA Change	-4.12	Deleterious	132	30	0.00 2	Damaging	3.17	92	Polr3e	0.538
pGM_7	17,47598 747,C,T, 0.281	ENSMU SP00000 040488	292	1	ACT [C/T]C C ACA	28 4	P	S	Single AA Change	-7.24	Deleterious	191	30	0	Damaging	2.93	152	Ccnd3	0.281
pGM_7	9,752960 82,C,G,0 .552	ENSMU SP00000 042229	174 2	1	AGA [C/G]A G ATT	14 87	Q	E	Single AA Change	-2.9	Deleterious	172	30	0.00 1	Damaging	2.91	131	Myo5c	0.552
pGM_7	6,256881 95,C,A,0 .632	ENSMU SP00000 052185	600	-1	TTC T[G/T] C CTC	30 1	C	F	Single AA Change	-8.81	Deleterious	102	30	0.00 8	Damaging	2.78	258	Gpr37	0.632

Table S1 (pGM\_2)

Sample ID	INPUT	PROTE IN_ID	LE NG TH	ST RA	CODON_CH ANGE	POS	RESID UE	RESID UE	TYPE	PROVEA N	PROVEA N PREDIC TION	#SEQ for PROV EAN	#CLUS TER for PROVE AN	SIF T SC	SIFT PREDI CTION	SIFT_M EDIAN_ INFO	#SEQ for SIFT PREDIC TION	GENE_ NAME	VAF
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				N D			R EF	A LT		SCO RE	(cutoff=- 2.5)	PREDI CTION	PREDI CTION	OR E	(cutoff =0.05)				
13496_L S1	5,108680 355,A,C	ENSMU SP00000 071577	643	1	TTG A[A/C] G TTG	21 6	K	T	Single AA Change	-3.64	Deleteriou s	77	30	0.01 8	Damagi ng	2.89	55	Idua	0.296
13496_L S1	X,96160 175,C,T	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleteriou s	266	30	0.00 0	Damagi ng	2.89	331	Msn	0.519
13497_L S2	5,121168 002,C,A	ENSMU SP00000 058757	597	-1	ACT G[G/T] G GAC	60	G	V	Single AA Change	-7.17	Deleteriou s	180	30	0.00 0	Damagi ng	2.88	200	Ptpn11	0.472
13497_L S2	7,141192 550,T,A	ENSMU SP00000 026572	189	-1	GGT C[A/T] A GAA	61	Q	L	Single AA Change	-6.55	Deleteriou s	388	30	0.00 4	Damagi ng	3.33	384	Hras	0.37
13497_L S2	11,96704 095,C,T	ENSMU SP00000 099443	355	1	AAG [C/T]G C TGG	13 1	R	C	Single AA Change	-7.01	Deleteriou s	120	30	0.00 0	Damagi ng	2.93	108	Skap1	0.343
13497_L S2	18,34331 758,G,T	ENSMU SP00000 072386	144	1	ATT T[G/T] T ATC	17	C	F	Single AA Change	-9.97	Deleteriou s	122	30	0.00 7	Damagi ng	2.79	142	Srp19	0.179
13499_L S3	8,836708 04,G,A	ENSMU SP00000 116235	951	-1	AAC [C/T]C G GAG	86 3	P	S	Single AA Change	-7.03	Deleteriou s	165	30	0.01 4	Damagi ng	2.87	196	Pkn1	0.1
13499_L S3	11,97711 247,G,A	ENSMU SP00000 099436	205	1	TAT [G/A]G G ATG	14 8	G	R	Single AA Change	-7.79	Deleteriou s	267	30	0.01 2	Damagi ng	2.78	366	Psm3	0.094
13499_L S3	17,38275 103,G,A	ENSMU SP00000 071767	312	1	ACA [G/A]A A TGT	11 1	E	K	Single AA Change	-3.94	Deleteriou s	472	30	0.00 5	Damagi ng	2.86	398	Olf138	0.429
13499_L S3	X,20560 078,G,A	ENSMU SP00000 023832	299	1	GAT [G/A]G G TTG	26 6	G	R	Single AA Change	-4.53	Deleteriou s	86	30	0.03 7	Damagi ng	2.84	75	Rgn	0.417
13499_L S3	X,96160 175,C,T	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleteriou s	266	30	0.00 0	Damagi ng	2.89	331	Msn	0.628

**Table S1 (pGM\_3)**

Sample ID	INPUT	PROTEIN_ID	LENGTH	STRAND	CODON_CHANGE	POS	RESIDUE_REF	RESIDUE_ALT	TYPE	PROVEAN SCORE	PROVEAN PREDICTION (cutoff=-2.5)	#SEQ for PROVEAN PREDICTION	#CLUSTER for PROVEAN PREDICTION	SIFT SCORE	SIFT PREDICTION (cutoff=0.05)	SIFT_MEDIAN_INFO	#SEQ for SIFT PREDICTION	GENE_NAME	VAF
Donor_173	1,9545762,C,A	ENSMU SP0000071955	365	1	CTG C[C/A]G ACC	80	P	Q	Single AA Change	-4.92	Deleterious	98	30	0.019	Damaging	2.85	75	Rrs1	0.4
Donor_173	10,80325846,G,T	ENSMU SP0000020340	655	-1	GAC [C/A]CT CTG	171	P	T	Single AA Change	-6.79	Deleterious	112	30	0.001	Damaging	2.80	385	Pcsk4	0.444
Donor_173	11,70724114,C,T	ENSMU SP0000072048	1112	1	GAG C[C/T]G CTG	578	P	L	Single AA Change	-7.69	Deleterious	205	30	0.025	Damaging	3.18	387	Kif1c	0.976
Donor_173	15,89187431,T,A	ENSMU SP0000077978	585	-1	ACC C[A/T]C GTG	261	H	L	Single AA Change	-10.14	Deleterious	124	30	0.003	Damaging	2.87	114	Dennd6b	0.971
Donor_173	16,36280539,T,C	ENSMU SP0000049068	97	1	CAA G[T/C]C GTC	47	V	A	Single AA Change	-3.23	Deleterious	112	30	0.033	Damaging	2.85	135	Stfa1	0.966
Donor_173	18,48046799,C,T	ENSMU SP0000075513	434	1	TCC [C/T]GT GGG	15	R	C	Single AA Change	-5.21	Deleterious	992	30	0.000	Damaging	3.80	358	Eno1b	0.457
Donor_173	2,32417228,G,A	ENSMU SP0000028160	514	-1	AAA A[C/T]A GGA	358	T	I	Single AA Change	-5.59	Deleterious	218	30	0.000	Damaging	2.83	274	Slc25a25	0.481
Donor_173	4,140798123,A,G	ENSMU SP0000026377	664	-1	GCC C[T/C]C TTT	193	L	P	Single AA Change	-4.59	Deleterious	178	30	0.003	Damaging	2.81	175	Padi3	1
Donor_173	7,103584415,C,T	ENSMU SP0000040319	318	1	GTG G[C/T]C ATC	131	A	V	Single AA Change	-3.91	Deleterious	426	30	0.000	Damaging	3.00	399	Olf167	0.409
173_2	8,55872839,C,A	ENSMU SP0000054292	763	-1	CTC AA[G/T]CAA	193	K	N	Single AA Change	-3.1	Deleterious	107	30	0.04	Damaging	2.79	93	Adam29	0.355
173_2	5,137530229,C,T	ENSMU SP0000031726	340	-1	CGT G[G/A]A CAC	53	G	E	Single AA Change	-6.67	Deleterious	398	30	0	Damaging	3.24	373	Gnb2	0.244
173_2	11,100413753,A,G	ENSMU SP0000065278	443	-1	CTT [T/C]A C AAC	221	Y	H	Single AA Change	-3.58	Deleterious	158	30	0	Damaging	2.8	165	Leprel4	0.132

173_2	1,748905 34,C,A	ENSMU SP00000 006721	197	-1	TCC G[G/T] A GCA	14 8	G	V	Single AA Change	-8.72	Deleterious	266	30	0	Damaging	2.83	283	Cryba2	0.120
173_3	15,10167 9985,C, G,0.113	ENSMU SP00000 023786	554	-1	GGA G[G/C] C TAT	80	G	A	Single AA Change	-2.6	Deleterious	366	30	0.18 2	Tolerated	3.19	230	Krt6b	0.113
173_3	2,891934 94,A,G,0 .463	ENSMU SP00000 097378	310	-1	GAC T[T/C] G TTC	18 0	L	S	Single AA Change	-4.84	Deleterious	511	30	0	Damaging	3.13	399	Olfrl226	0.463
173_3	7,107181 842,C,T, 0.435	ENSMU SP00000 081819	993	1	CAA A[C/T] G GTA	82	T	M	Single AA Change	-4.99	Deleterious	138	30	0.00 5	Damaging	2.78	51	Nlrp14	0.435
173_3	X,96160 175,C,T, 0.917	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.917
173_4	17,19394 163,C,T, 0.319	ENSMU SP00000 135236	856	1	GCA A[C/T] G TCT	71 5	T	M	Single AA Change	-4.87	Deleterious	166	30	0.02 2	Damaging	2.74	240	Vmn2r99	0.319
173_4	9,194776 83,T,G,0 .270	ENSMU SP00000 076569	315	-1	CTC A[A/C] G TTG	18 9	K	T	Single AA Change	-5.53	Deleterious	181	30	0.00 1	Damaging	3.13	397	Olfrl850	0.270
173_4	18,78859 084,C,G, 0.109	ENSMU SP00000 025430	153 5	-1	CCT C[G/C] A GTC	40 9	R	P	Single AA Change	-2.51	Deleterious	92	22	0.00 3	Damaging	3.76	39	Setbp1	0.109
173_4	9,762545 51,G,A,0 .292	ENSMU SP00000 058230	460	-1	ATT [C/T]C T CAA	18 6	P	S	Single AA Change	-7.22	Deleterious	149	30	0	Damaging	2.88	86	Hcrtr2	0.292
173_4	2,259004 00,C,A,0 .214	ENSMU SP00000 039058	123 8	1	TGG G[C/A] T GTG	45 8	A	D	Single AA Change	-5.76	Deleterious	155	30	0	Damaging	2.85	179	Kcnt1	0.214
173_4	5,219978 93,T,G,0 .146	ENSMU SP00000 058025	345 9	-1	CTG C[A/C] G TTC	13 03	Q	P	Single AA Change	-2.83	Deleterious	81	30	0	Damaging	2.91	63	Reln	0.146
173_4	9,219597 66,A,C,0 .162	ENSMU SP00000 006397	507	-1	AAC [T/G]T C CAG	30 3	F	V	Single AA Change	-3.14	Deleterious	148	30	0	Damaging	2.83	52	Epor	0.162
173_4	X,96160 175,C,T, 0.694	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.694
173_4	2,165828 348,G,A, 0.125	ENSMU SP00000 018050	117 9	-1	CTG T[C/T] C GAC	42 7	S	F	Single AA Change	-2.6	Deleterious	171	30	0	Damaging	3.41	146	Zmynd8	0.125

173_4	8,125464 224,A,G, 0.273	ENSMU SP00000 104405	172 2	-1	ATG A[T/C] T GAC	10 09	I	T	Single AA Change	-3.63	Deleterious	154	30	0.04 6	Damaging	2.85	132	Sipa112	0.273
173_4	11,12071 5566,G, A,0.231	ENSMU SP00000 026139	670	1	CTG [G/A]C C CTG	16 7	A	T	Single AA Change	-2.89	Deleterious	67	30	0	Damaging	2.94	46	Lrrc45	0.231
173_4	8,950622 77,T,A,0 .120	ENSMU SP00000 053972	876	1	TTC A[T/A] C GAC	32 1	I	N	Single AA Change	-6.18	Deleterious	72	30	0	Damaging	2.81	59	Ccdc135	0.12
173_5	16,88773 718,T,C, 0.109	ENSMU SP00000 062370	200	-1	TCT [A/G]G A AGC	14 5	R	G	Single AA Change	-6.11	Deleterious	115	30	0.04 4	Damaging	3.01	126	2310057 N15Rik	0.109
173_5	17,23856 171,G,A, 0.400	ENSMU SP00000 050389	334	1	GTC T[G/A] C CTC	16 5	C	Y	Single AA Change	- 10.82	Deleterious	97	30	0	Damaging	2.81	86	Prss32	0.400
173_5	X,18261 559,C,T, 0.109	ENSMU SP00000 045862	140 1	1	TTA [C/T]A T CAA	95 7	H	Y	Single AA Change	-4.43	Deleterious	309	30	0.00 2	Damaging	3.39	309	Kdm6a	0.109
173_5	X,96160 175,C,T, 0.862	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.862
173_9	7,848335 6,T,C,0.2 58	ENSMU SP00000 129466	852	-1	ACA G[A/G] C ATA	31 1	D	G	Single AA Change	-5.16	Deleterious	231	30	0.01 8	Damaging	2.77	265	Vmn2r45	0.258
173_9	6,396431 35,C,T,0. 174	ENSMU SP00000 002487	804	-1	TCT G[G/A] G TCA	50 3	G	E	Single AA Change	-7.58	Deleterious	255	30	0	Damaging	2.85	228	Braf	0.174
173_9	11,12045 0558,C,T ,0.145	ENSMU SP00000 026452	87	-1	GGA [G/A]G A CCA	19	G	R	Single AA Change	-4.75	Deleterious	103	14	0.00 1	Damaging	3.73	84	Pde6g	0.145
173_9	2,733821 32,C,T,0. 606	ENSMU SP00000 075788	868	-1	TTT G[G/A] C ATA	49	G	D	Single AA Change	-4.22	Deleterious	90	30	0.00 5	Damaging	2.86	65	Gpr155	0.606
173_9	X,96160 175,C,T, 0.563	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.563
173_10	14,54953 418,C,A, 0.663	ENSMU SP00000 080538	193 8	-1	GAG GA[G/ T] ATG	93 3	E	D	Single AA Change	-2.52	Deleterious	529	30	0.01 5	Damaging	3.89	395	Myh6	0.663
173_10	X,96160 175,C,T, 0.958	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleterious	266	30	0	Damaging	2.89	331	Msn	0.958

Table S1 (pGM\_4)

Sample ID	INPUT	PROTEIN_ID	LENGTH	STRAND	CODON_CHANGE	POS	RESIDUE_REF	RESIDUE_ALT	TYPE	PROVEAN_SCORE	PROVEAN_PREDICTION (cutoff=-2.5)	#SEQ for PROVEAN_PREDICTION	#CLUSTER for PROVEAN_PREDICTION	SIFT_SCORE	SIFT_PREDICTION (cutoff=0.05)	SIFT_MEDIAN_INFO	#SEQ for SIFT_PREDICTION	GENE_NAME	VAF
Donor_174	10,80325846,G,T	ENSMU SP0000020340	655	-1	GAC [C/A]CT CTG	171	P	T	Single AA Change	-6.79	Deleterious	112	30	0.001	Damaging	2.80	385	Pcsk4	0.969
Donor_174	11,70724114,C,T	ENSMU SP0000072048	1112	1	GAG C[C/T]G CTG	578	P	L	Single AA Change	-7.69	Deleterious	205	30	0.025	Damaging	3.18	387	Kif1c	0.969
Donor_174	15,89187431,T,A	ENSMU SP0000077978	585	-1	ACC C[A/T]C GTG	261	H	L	Single AA Change	-10.14	Deleterious	124	30	0.003	Damaging	2.87	114	Dennd6b	0.947
Donor_174	16,36280539,T,C	ENSMU SP0000049068	97	1	CAA G[T/C]C GTC	47	V	A	Single AA Change	-3.23	Deleterious	112	30	0.033	Damaging	2.85	135	Stfa1	0.962
Donor_174	18,48046799,C,T	ENSMU SP0000075513	434	1	TCC [C/T]G T GGG	15	R	C	Single AA Change	-5.21	Deleterious	992	30	0.000	Damaging	3.80	358	Eno1b	0.446
Donor_174	19,7096625,G,A	ENSMU SP00000109010	674	-1	AGC [C/T]G G AAC	186	R	W	Single AA Change	-4.35	Deleterious	242	30	0.001	Damaging	2.93	123	Flrt1	0.549
Donor_174	2,32417228,G,A	ENSMU SP0000028160	514	-1	AAA A[C/T]A GGA	358	T	I	Single AA Change	-5.59	Deleterious	218	30	0.000	Damaging	2.83	274	Slc25a25	0.489
Donor_174	4,140798123,A,G	ENSMU SP0000026377	664	-1	GCC C[T/C]C TTT	193	L	P	Single AA Change	-4.59	Deleterious	178	30	0.003	Damaging	2.81	175	Padi3	0.938
Donor_174	7,10050337,T,A	ENSMU SP0000074476	861	-1	ACT A[A/T]A AAC	70	K	I	Single AA Change	-4.16	Deleterious	211	30	0.004	Damaging	2.79	233	Vmn2r50	0.988
Donor_174	9,44249891,A,G	ENSMU SP0000034618	498	-1	TTG [T/C]G C CAT	158	C	R	Single AA Change	-9.95	Deleterious	203	30	0.000	Damaging	2.86	63	Pdzd3	0.889
Donor_174	X,96160175,C,T	ENSMU SP00000113071	577	1	CGG [C/T]G C AAG	295	R	C	Single AA Change	-7.92	Deleterious	266	30	0.000	Damaging	2.89	331	Msn	0.233

174_4	11,11654 4465,G, A,0.488	ENSMU SP00000 080791	128 8	-1	TCC T[C/T] C CAG	49 9	S	F	Single AA Change	-2.91	Deleteriou s	88	30	0.00 6	Damagi ng	3.21	51	Ubc2o	0.488
174_4	17,70846 288,G,C, 0.208	ENSMU SP00000 060512	272	-1	CTG [C/G]C C AAG	43	P	A	Single AA Change	-7.64	Deleteriou s	142	30	0.01	Damagi ng	2.97	156	Tgifl	0.208
174_4	X,96160 175,C,T, 0.968	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleteriou s	266	30	0	Damagi ng	2.89	331	Msn	0.968
174_5	15,39506 980,A,C, 0.101	ENSMU SP00000 048719	157 2	1	ATA [A/C]G T GAC	93 7	S	R	Single AA Change	-4.03	Deleteriou s	171	30	0.00 1	Damagi ng	3.1	174	Rims2	0.101
174_5	7,437210 93,T,G,0 .424	ENSMU SP00000 065308	276	1	CGA C[T/G] T CTC	60	L	R	Single AA Change	-3.15	Deleteriou s	276	30	0	Damagi ng	2.82	162	Klk13	0.424
174_5	1,153258 113,A,G, 0.111	ENSMU SP00000 027752	160 7	-1	TCT [T/C]A C TAT	27 1	Y	H	Single AA Change	-4.36	Deleteriou s	139	30	0	Damagi ng	2.82	68	Lamc1	0.111
174_8	3,267775 38,C,A,0 .101	ENSMU SP00000 043378	571	1	CGA AA[C/ A] CAT	26 5	N	K	Single AA Change	-2.83	Deleteriou s	67	10	0	Damagi ng	3.89	40	Spata16	0.101
174_8	3,389494 86,G,T,0 .552	ENSMU SP00000 061836	498 1	1	GAT [G/T]A C AGC	17 85	D	Y	Single AA Change	-3.74	Deleteriou s	79	30	0.03 2	Damagi ng	2.85	53	Fat4	0.552
174_8	11,10020 5048,C,T ,0.527	ENSMU SP00000 007272	484	-1	CTG C[G/A] C AGG	22 8	R	H	Single AA Change	-4.42	Deleteriou s	442	30	0.00 6	Damagi ng	2.92	396	Krt14	0.527
174_8	X,96160 175,C,T, 0.938	ENSMU SP00000 113071	577	1	CGG [C/T]G C AAG	29 5	R	C	Single AA Change	-7.92	Deleteriou s	266	30	0	Damagi ng	2.89	331	Msn	0.938
174_10	1,664383 15,A,C,0 .400	ENSMU SP00000 024639	467	1	GCT AA[A/ C] GTT	37 9	K	N	Single AA Change	-4.45	Deleteriou s	231	30	0	Damagi ng	3.31	364	Map2	0.4
174_10	2,603300 85,T,A,0 .379	ENSMU SP00000 028362	172 3	-1	GCC A[A/T] G TTG	92 6	K	M	Single AA Change	-2.62	Deleteriou s	167	30	0.00 1	Damagi ng	2.92	69	Ly75	0.379
174_10	6,100232 417,A,G, 0.268	ENSMU SP00000 098677	228	-1	CGG C[T/C] G AAG	14 8	L	P	Single AA Change	-6.44	Deleteriou s	128	30	0	Damagi ng	2.93	122	Rybp	0.268
174_10	7,131112 126,T,C, 0.365	ENSMU SP00000 081556	194 6	1	TCC A[T/C] G GGC	16 30	M	T	Single AA Change	-2.53	Deleteriou s	66	30	0.01	Damagi ng	2.97	52	Dmbt1	0.365

174_10	1,152544 364,T,C, 0.140	ENSMU SP00000 027760	768	-1	CGG G[A/G] G CTA	37 6	E	G	Single AA Change	-6.76	Deleterious	182	30	0.00 1	Damaging	2.9	139	Rgl1	0.14
174_10	6,650993 09,A,T,0 .140	ENSMU SP00000 031984	102 1	1	AGA AA[A/ T] ATG	77 5	K	N	Single AA Change	-4.51	Deleterious	105	30	0.00 2	Damaging	2.91	99	Smarcad 1	0.14
174_10	5,121167 955,C,T, 0.137	ENSMU SP00000 058757	597	-1	GCT [G/A]A A CTG	76	E	K	Single AA Change	-3.45	Deleterious	180	30	0.00 6	Damaging	2.88	198	Ptpn11	0.137
174_10	18,71587 950,A,C, 0.146	ENSMU SP00000 073094	142 7	-1	CGT [T/G]T G AGC	44 7	L	V	Single AA Change	-2.76	Deleterious	134	30	0.00 2	Damaging	2.86	116	Dcc	0.146
174_10	6,927774 60,C,T,0. 178	ENSMU SP00000 109065	193 1	-1	TGC [G/A]G C GGT	19 12	G	S	Single AA Change	-4.32	Deleterious	111	30	0	Damaging	3.05	76	Adamts9	0.178
174_10	8,450301 90,G,T,0 .119	ENSMU SP00000 096394	459 0	1	GGA G[G/T] T GGG	31 05	G	V	Single AA Change	-5.56	Deleterious	142	30	0	Damaging	2.91	112	Fat1	0.119
174_10	X,48563 691,T,G, 0.700	ENSMU SP00000 072138	733	-1	AAA A[A/C] T AAT	32 5	N	T	Single AA Change	-4.9	Deleterious	223	30	0.00 1	Damaging	2.83	245	Zfp280c	0.7
174_10	11,49630 297,C,T, 0.130	ENSMU SP00000 020617	136 3	1	GGG [C/T]G C CAC	37 8	R	C	Single AA Change	-3.6	Deleterious	191	30	0.00 1	Damaging	2.83	134	Flt4	0.13
174_10	17,67800 766,T,C, 0.389	ENSMU SP00000 043957	308 3	1	AAA G[T/C] C GCC	21 25	V	A	Single AA Change	-3.55	Deleterious	107	30	0.00 2	Damaging	2.88	90	Lama1	0.389

Somatic mutations (VAF>0.1) identified in AML originating from CLP, GMLP and pGM cells (cohort 1) and for paired parental/MLL-ENL AML samples by whole genome or whole exome sequencing (cohorts 2-4; n = 25). INPUT column contains information of Chromosome, Position, Reference allele and Alternative allele. SIFT: Sorting Intolerant from Tolerant algorithm, tool used for detecting deleterious amino acid substitutions. PROVEAN: Protein Variation Effect Analyzer, tool that provides predictions for any type of protein sequence variations.



**Table S2.****833C>T mutant *Msn* allele reads in ultradeep targeted sequencing (n=3 per group)**

<b>Sample</b>	<b>Total sequences</b>	<b>C/T Mut sequences</b>	<b>MAF</b>
<b>MUT/WT 1/100</b>	47,027	412	0.008760925
<b>MUT/WT 1/1000</b>	36,142	43	0.001189752
<b>WT</b>	40,429	10	0.000247347
<b>MLL ENL #1</b>	38,505	4	0.000103883
<b>MLL ENL #2</b>	41,583	4	0.000096193
<b>MLL ENL #3</b>	38,674	8	0.000206857
<b>C57BL/6N #1</b>	38,312	6	0.000156609
<b>C57BL/6N #2</b>	38,852	8	0.00020591
<b>C57BL/6N #3</b>	40,647	4	0.000098408

833 C>T mutant *Msn* allele reads and their mutant allele frequency (MAF) from the targeted amplicon sequencing.

**Table S3.****High confidence interactors of WT or C295 mutant MSN**

<b>Uniprot.ID</b>	<b>Gene.names</b>	<b>Unique.peptides</b>
P26041	Msn	54
Q80X90	Flnb	35
P24527	Lta4h	28
P29341	Pabpc1	28
Q3U1J4	Ddb1	26
P63017	Hspa8	22
O55029	Copb2	22
P25206	Mcm3	20
Q91V92	Acly	18
Q9WTM5	Ruvbl2	18
Q9WV32	Arpc1b	17
O89053	Coro1a	16
P61982	Ywhag	12
Q6ZWX6	Eif2s1	11
P97351	Rps3a	11
Q9EPU0	Upf1	11
P60122	Ruvbl1	11
Q3UP87	Elane	10
Q921F2	Tardbp	10
P97311	Mcm6	10
O08573	Lgals9	10
Q99KP6	Prpf19	10
P11835	Itgb2	10
Q6ZWN5	Rps9	10
Q9CXW4	Rpl11	10
P63158	Hmgb1	10
P70677	Casp3	9
Q8R081	Hnrnp1	9
P63037	Dnaja1	9
P61358	Rpl27	8
Q8N7N5	Dcaf8	8
P62889	Rpl30	8
P23198	Cbx3	8
P62245	Rps15a	8
P26043	Rdx	7
Q60604	Scin	7
O55023	Impa1	7
Q5SWU9	Acaca	7

Q8VDJ3	Hdlbp	7
P51859	Hdgf	7
Q9QUM9	Psma6	6
Q9CXY6	Ilf2	6
Q62446	Fkbp3	6
P50431	Shmt1	6
O70133	Dhx9	6
Q62351	Tfre	6
Q99MD9	Nasp	6
Q9CZU6	Cs	6
Q8CDN6	Txn11	6
Q91V12	Acot7	6
Q9CQ65	Mtap	6
Q9Z0N1	Eif2s3x	6
P14148	Rpl7	6
Q61096	Prtn3	5
Q9CQQ7	Atp5f1	5
P70372	Elav11	5
P70441	Slc9a3r1	5
P63085	Mapk1	5
Q8BL97	Srsf7	5
Q9JII6	Akr1a1	5
P28352	Apex1	5
Q8VEE4	Rpa1	5
O55135	Eif6	5
P62320	Snrpd3	5
Q8CAQ8	Immt	5
Q62426	Cstb	5
P54227	Stmn1	4
P15379	Cd44	4
Q4VAA2	Cdv3	4
P62317	Snrpd2	4
Q8VDF2	Uhrf1	4
P24063	Itgal	4
P54822	Adsl	4
Q9R1P4	Psma1	4
Q64261	Cdk6	4
P37913	Lig1	4
Q6ZWY8	Tmsb10	4
Q9D1R9	Rpl34	3
P61290	Psme3	3
Q9JK81	Myg1	3

Q9CZY3	Ube2v1	3
Q8K183	Pdxk	3
P17156	Hspa2	3
P61222	Abce1	3
Q61584	Fxr1	3
P83870	Phf5a	3
Q6ZWR6	Syne1	2
A2BH40	Arid1a	2
P18572	Bsg	2
Q8CCS6	Pabpn1	2
Q9DAK9	Phpt1	2
Q8VBT0	Tmx1	2
P53810	Pitpna;Pitpnb	2
Q9QYS9	Qki	2
Q9JKB3	Ybx3	2
Q99KR7	Ppif	2
Q6A028	Swap70	2
Q9WVA2	Timm8a1;Timm8a2	2
Q9Z2N8	Actl6a	2
Q3UVK0	Ermp1	2
Q8C570	Rae1	2
Q9Z2I9	Sucla2	2
Q8BIQ5	Cstf2	2
O55142	Rpl35a	2
Q8CF17	Polr2b	2
P20060	Hexb	2
Q91VR5	Ddx1	2
Q60676	Ppp5c	2
P49290	Epx	1
P70288	Hdac2	1
P35991	Btk	1
P55821	Stmn2	1
Q8BJ71	Nup93	1
O35857	Timm44	1
Q78ZA7	Nap114	1
Q9R0U0	Srsf10	1

Proteins with significantly higher abundance in WT or C295 mutant MSN compared to background control.

**Table S4. Sequences of primers for PCR used in this study**

Primers	Sequence 5' to 3'	SOURCE	IDENTIFIER
Primer for Assessment of clonality			
Assessment of clonality Fw	ACGATACAAGGCTGTTAGAGAGA	Integrated DNA Technologies	Own design
Assessment of clonality Rev	CGGTGCCACTTTTTCAAGTT	Integrated DNA Technologies	Own design
Primers for cloning			
MigR1 Msn assembly Fw	ACGTTAGGGGGGGGGGGCGGATGCCGAAGACG	Integrated DNA Technologies	Own design
MigR1 Msn assembly Rev	AGGCGCCGGAATTAGATCTCCTACATGGACTCA	Integrated DNA Technologies	Own design
MigR1 Msn R295C substitution mutagenesis Fw	CATGCGTCGGIGCAAGCCTGA	Integrated DNA Technologies	Own design
MigR1 Msn R295C substitution mutagenesis Rev	TACAGCTCATGATTTCCCATGCAC	Integrated DNA Technologies	Own design
MigR1 Msn T558A substitution mutagenesis Fw	CAAATACAAGGCCCTGCGCCA	Integrated DNA Technologies	Own design
MigR1 Msn T558A substitution mutagenesis Rev	TCTCGTCCCAGTCGCATG	Integrated DNA Technologies	Own design
MigR1 Msn T558D substitution mutagenesis Fw	CAAATACAAGGACCTGCGCCAGATCC	Integrated DNA Technologies	Own design
MigR1 Msn T558D substitution mutagenesis Rev	TCTCGTCCCAGTCGCATG	Integrated DNA Technologies	Own design
MigR1 Msn 3xFlag insertion mutagenesis Fw	CATGACATCGATTACAAGGATGACGAT	Integrated DNA Technologies	Own design
MigR1 Msn 3xFlag insertion mutagenesis Rev	ATCTTTATAATCACCGTCATGGTCTTTGTAGTCCA	Integrated DNA Technologies	Own design
Primers for qRT-PCR			
Msn Fw	GGAGGTAAGAGGACTGGTGTC	Integrated DNA Technologies	Own design
Msn Rev	TTCCACTCCCTAAGCAAGCC	Integrated DNA Technologies	Own design
$\beta$ Actin Fw	CCACAGCTGAGAGGCAAATC	Integrated DNA Technologies	Own design
$\beta$ Actin Rev	CTTCTCCAGGGAGGAAGAGG	Integrated DNA Technologies	Own design
Meis1 Fw	AGTTGGCACAAAGATACAGGAC	Integrated DNA Technologies	Own design
Meis1 Rev	GGGCTGCACTATTCTTCTCC	Integrated DNA Technologies	Own design
Hoxa9 Fw	ACAATGCCGAGAATGAGAGC	Integrated DNA Technologies	Own design
Hoxa9 Rev	GTTCCAGCGTCTGGTGTTTT	Integrated DNA Technologies	Own design