

## SUPPLEMENTARY MATERIALS

### Supplemental Figure Legends

**Supplemental Figure 1. *SF3B1* is frequently mutated in patients with RARS and RARS-T.** We performed Sanger sequencing on exons 13, 14, 15, and 16 of *SF3B1* in 456 patients. Patients are divided in 4 groups: (A) MDS (n=93), (B) MDS/MPN (n=105), (C) AML (n=94), and (D) Others (n=164). Bar histograms show the frequency of *SF3B1* mutations. White bars and black bars indicate wild type and mutant patients, respectively. The frequency of *SF3B1* mutations is higher in patients with RARS (68%) and RARS-T (81%) compared to the other groups. (E) Schematic distribution of *SF3B1* mutations in different diseases according to 2008 World Health Organization criteria. Each color represents a specific mutation.

MDS, myelodysplastic syndromes; MPN, myeloproliferative neoplasms; AML, acute myeloid leukemia.

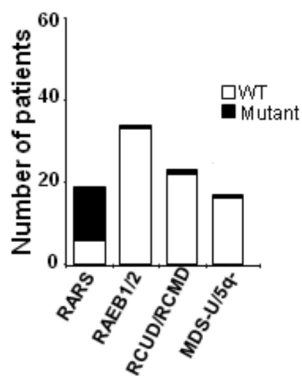
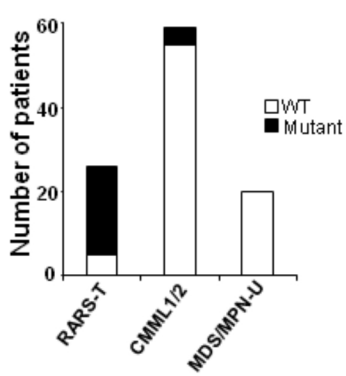
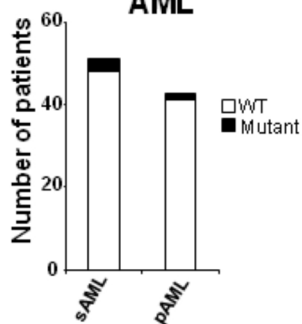
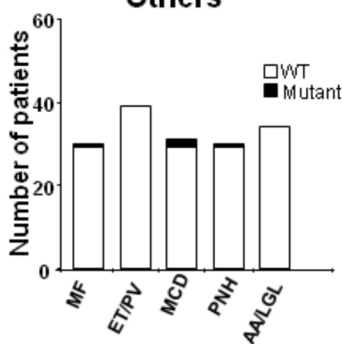
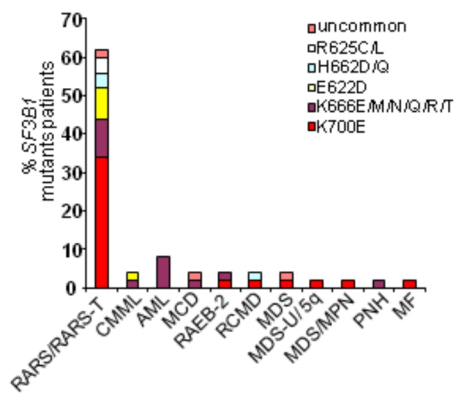
**Supplemental Figure 2. Human Colony Forming-Units Cell Assay.** Human clonogenic progenitor cells with and without different doses of meayamycin (2, 10, 50nM) were analyzed for the presence of ring sideroblasts (RS) after 2 weeks of culture. Bar histogram represents the percentage of RS calculated by scoring 200 erythroid cells per concentration of meayamycin in representative experiment.

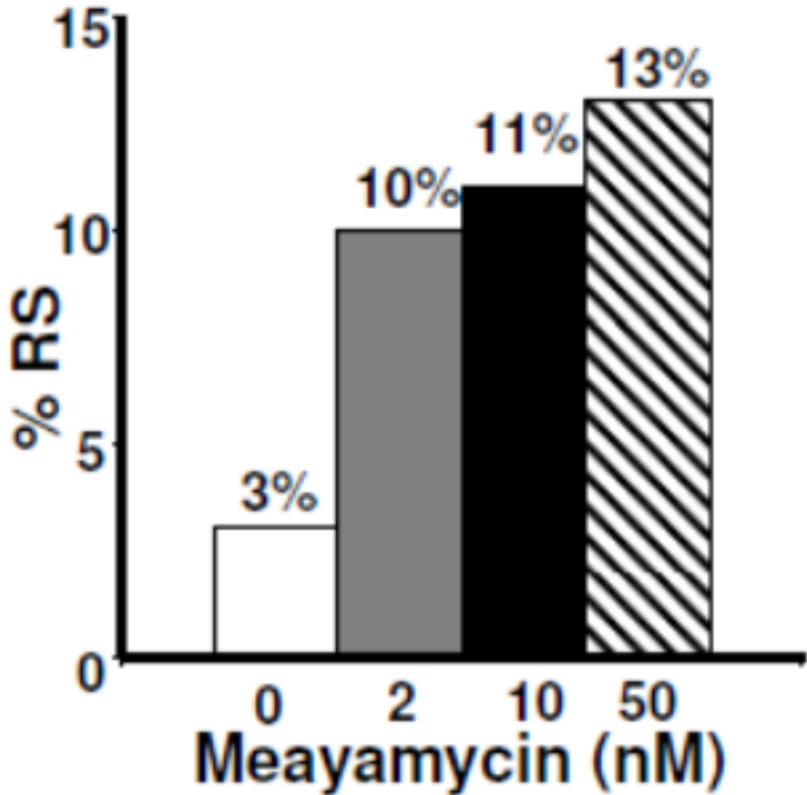
**Supplemental Figure 3. *SF3B1* mutations predicts for better overall survival.** Overall survival calculated by univariate analysis at time of sampling is presented for (A) MDS, (B) MDS/MPN, and (C) RARS/RARS-T groups. Blue and

magenta lines represent wild type (WT) and mutant patients, respectively.  $P \leq .05$  is considered statistically significant.

**Supplemental Table 1. List of genes showing differential gene expression between *SF3B1* mutant and normal samples.** Differential gene expression was tested on 12,870 reference genes for differential expression. One hundred thirty genes were found to be differentially expressed using a False Discovery Rate (FDR) level of 0.05. Ninety-four % of these genes were under-expressed in *SF3B1* mutant compared to normal samples.

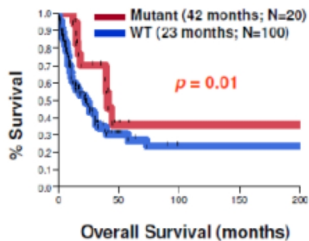
**Supplemental Table 2. List of gene sets showing over and under representation of differential gene expression.** MSigDB database version 3.0 (<http://www.broadinstitute.org/gsea/msigdb/index.jsp>) was used to define gene set collections (c2-c5) of under and over represented genes. Adjusted  $P < 0.05$  is considered significant for each gene set.

**A****MDS****B****MDS/MPN****C****AML****D****Others****E**



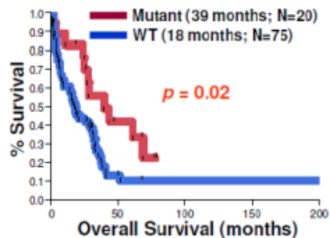
a)

## MDS



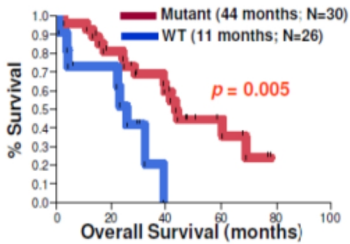
b)

## MDS/MPN



c)

## RARS/RARS-T



Supplemental Table 1. List of genes showing differential gene expression in SF3B1 mutant versus normal samples

Gene Name	Chr	Gene location	Adjust P-value	BaseM	BaseN	Log2fold(Mutant/Healthy Donor)	P-value
HBG1	11	5269502-5271087	3.49E-05	15068	121	6.77	1.11E-07
SLC7A5P1	16	29624424-29625038	1.35E-04	686	4	5.69	4.94E-07
PTTG3P	8	67679634-67680240	2.13E-03	181	0	5.17	1.08E-05
FAM57B	16	30035749-30042186	4.40E-03	6502	0	10.10	2.53E-05
LOC100271831	16	30125433-30125826	1.51E-02	1679	0	8.16	1.08E-04
RUNCDC3A	17	42385927-42396037	2.31E-02	225	4	4.02	1.90E-04
FLJ42393	3	187896331-187898596	2.42E-02	448	0	6.32	2.03E-04
GDPD3	16	30116132-30124878	4.06E-02	94	0	4.27	3.79E-04
DEFA4	8	6793345-6795786	5.50E-19	6	24454	-10.56	4.28E-23
PRG3	11	57144243-57148623	6.33E-17	1	5799	-9.50	9.84E-21
EPX	17	56270089-56282534	2.14E-14	4	4592	-8.50	5.00E-18
RNASE3	16	21359562-21360506	1.09E-13	6	5527	-8.51	3.38E-17
CORO1A	14	30194926-30200396	9.20E-13	2	1986	-7.48	4.06E-16
PRG2	11	57154835-57158130	9.20E-13	97	43622	-9.31	4.29E-16
CEACAM6	19	42259398-42276113	1.02E-12	8	4279	-7.88	6.37E-16
ELANE	19	852291-856244	1.02E-12	167	71946	-9.65	5.89E-16
DEFA3	8	6873395-6875816	2.16E-12	4	2404	-7.57	1.51E-15
PPP4C	16	30087384-30096688	6.24E-12	2	1372	-7.31	4.85E-15
CAMP	3	48264862-48266975	2.29E-11	41	10636	-7.59	1.96E-14
LTF	3	46477497-46506395	6.03E-11	405	93610	-8.38	5.62E-14
CTSG	14	25042725-25045466	7.22E-11	37	9227	-7.86	7.29E-14
RNASE2	14	21423630-21424594	4.53E-10	62	10796	-7.22	4.93E-13
TCN1	11	59620281-59634041	6.73E-10	3	985	-6.37	7.85E-13
PRTN3	19	840985-848175	7.21E-10	247	41679	-8.62	8.97E-13
AZU1	19	827831-832017	9.44E-10	68	11331	-7.70	1.25E-12
BPI	20	36932552-36965905	1.75E-09	37	5356	-6.75	2.45E-12
OLR1	12	10310899-10324790	1.09E-08	3	724	-5.93	1.61E-11
CLC	19	40221896-40228668	1.12E-08	21	2835	-6.65	1.74E-11
SGK3	8	67624891-67774255	6.05E-08	0	335	-6.02	9.88E-11
SLPI	20	43880879-43883206	7.85E-08	3	670	-5.71	1.34E-10
MMP8	11	102582526-102595685	1.33E-07	67	5691	-6.64	2.38E-10
LCN2	9	130911732-130915734	1.82E-07	45	3174	-5.77	3.38E-10
MMP9	20	44637547-44645199	2.09E-07	27	2196	-5.79	4.06E-10
CEACAM8	19	43084395-43099082	2.12E-07	50	3734	-5.90	4.29E-10
MS4A3	11	59824101-59838587	6.24E-07	20	1717	-6.65	1.31E-09
CRISP3	6	49695092-49712056	1.11E-06	28	1944	-5.83	2.41E-09
C16orf54	16	29753786-29757340	1.46E-06	0	240	-5.56	3.29E-09
IL8	4	74606275-74609431	1.71E-06	385	19694	-5.80	3.98E-09
S100P	4	6695566-6698896	1.86E-06	14	941	-5.21	4.49E-09
MPO	17	56347217-56358296	3.12E-06	1607	81048	-7.58	7.76E-09
SRGN	10	70847828-70864565	6.54E-06	2673	92897	-5.17	1.68E-08
TMEM176B	7	150488378-150497621	8.17E-06	17	822	-5.06	2.16E-08

PGLYRP1	19	46522412-46526556	1.02E-05	6	489	-4.88	2.87E-08
SDCX	8	97505882-97624037	1.02E-05	1	230	-5.08	2.83E-08
ALOX15	17	4534221-4544960	1.47E-05	2	275	-5.06	4.24E-08
HP	16	72088508-72094957	2.14E-05	26	1169	-4.98	6.31E-08
CCL7	17	32597240-32599255	2.90E-05	0	172	-5.11	9.02E-08
S100A8	1	153362509-153363549	2.90E-05	8552	243742	-4.85	8.80E-08
TXNIP	1	145438462-145442626	3.97E-05	192	6874	-6.79	1.29E-07
S100A12	1	153346184-153348075	5.51E-05	607	15905	-4.69	1.84E-07
LYZ	12	69742134-69748013	8.78E-05	36753	854523	-4.60	3.00E-07
LPP	3	187930721-188608459	1.20E-04	5	316	-4.45	4.20E-07
IL1R2	2	102608306-102644880	1.22E-04	10	525	-4.80	4.36E-07
B3GNT5	3	182971032-182991178	1.52E-04	69	1976	-4.65	5.67E-07
FCGR3B	1	161592990-161601158	1.66E-04	42	999	-4.74	6.30E-07
S100A9	1	153330330-153333502	1.79E-04	3901	79729	-4.43	6.96E-07
OLFM4	13	53602972-53626186	2.18E-04	12	519	-4.51	8.65E-07
CHI3L1	1	203148059-203155922	3.82E-04	24	812	-5.49	1.55E-06
FCAR	19	55385549-55401839	6.02E-04	116	2410	-4.21	2.48E-06
CD24	Y	21152526-21154705	7.14E-04	62	1409	-4.25	2.99E-06
PLAU	10	75670862-75677256	7.79E-04	11	399	-4.17	3.33E-06
ALPL	1	21835858-21904904	1.11E-03	2	178	-4.52	4.82E-06
CHIT1	1	203185207-203198860	1.29E-03	6	286	-4.34	5.73E-06
NCRNA00152	2	87754974-87821028	1.33E-03	0	108	-4.51	5.99E-06
MGAM	7	141695679-141806546	1.35E-03	18	466	-3.97	6.18E-06
ANXA3	4	79472742-79531602	1.37E-03	72	1463	-4.18	6.44E-06
GPR97	16	57702157-57723288	1.37E-03	46	1045	-4.39	6.49E-06
TNFRSF12A	16	3070313-3072381	1.43E-03	19	450	-3.96	6.90E-06
IL1RL1	2	102953717-102961180	1.77E-03	0	123	-4.33	8.67E-06
TMEM176A	7	150497854-150502208	1.82E-03	2	152	-4.26	9.06E-06
EMP1	12	13349602-13369707	2.22E-03	21	487	-3.89	1.14E-05
MAP3K8	10	30722866-30750761	2.33E-03	147	2166	-3.82	1.22E-05
CD177	19	43857825-43867479	2.53E-03	8	284	-4.12	1.34E-05
ALOX5AP	13	31309669-31338556	2.69E-03	345	5130	-3.83	1.44E-05
PLAUR	19	44152732-44174502	3.10E-03	688	9914	-3.83	1.69E-05
MME	3	154797436-154901518	3.35E-03	8	263	-3.87	1.85E-05
HDC	15	50534148-50557926	3.79E-03	4	199	-4.41	2.12E-05
CA4	17	58227302-58236904	4.40E-03	0	90	-4.28	2.53E-05
IFNGR1	6	137518621-137540567	4.54E-03	586	7212	-3.65	2.64E-05
NAMPT	7	105888734-105925638	5.11E-03	1321	15379	-3.64	3.02E-05
BCL2A1	15	80253233-80263643	5.60E-03	245	2727	-3.85	3.35E-05
HBEGF	5	139712429-139726188	6.04E-03	40	727	-3.90	3.66E-05
TREM1	6	41243712-41254457	6.12E-03	60	808	-3.67	3.76E-05
CHD1L	1	146714291-146767441	6.89E-03	32	493	-3.65	4.29E-05
SAMSN1	21	15857549-15918664	7.08E-03	289	3314	-3.55	4.46E-05
RETN	19	7733972-7735340	7.14E-03	19	403	-3.73	4.55E-05
ANPEP	15	90328127-90358072	7.51E-03	227	2963	-3.64	4.85E-05

THBD	20	23026271-23030301	7.65E-03	10	273	-3.74	4.99E-05
MAPK3	16	30125427-30134630	8.36E-03	0	97	-4.03	5.52E-05
ANXA1	9	75766781-75785307	8.40E-03	2803	31070	-3.48	5.61E-05
PCOLCE2	3	142536712-142607934	9.57E-03	0	79	-4.12	6.47E-05
LRG1	19	4537228-4540036	1.04E-02	24	413	-3.52	7.14E-05
IL1RAP	3	190231840-190348071	1.16E-02	19	341	-3.49	8.02E-05
SPN	16	29674580-29681821	1.24E-02	40	612	-3.58	8.70E-05
OSM	22	30658821-30662840	1.29E-02	80	1134	-3.85	9.11E-05
C19orf59	19	7741943-7744719	1.61E-02	123	1360	-3.33	1.17E-04
SERPINE1	7	100770379-100782546	1.61E-02	21	308	-3.57	1.18E-04
ALDOA	16	30077044-30081734	1.64E-02	1002	10163	-3.32	1.24E-04
CXCR1	2	219027570-219031716	1.64E-02	25	362	-3.41	1.25E-04
FCN1	9	137801436-137809806	1.64E-02	5124	47277	-3.32	1.23E-04
ORM1	9	117085303-117088757	1.64E-02	3	134	-3.57	1.25E-04
FPR2	19	52264453-52273777	1.70E-02	80	945	-3.33	1.31E-04
QPCT	2	37571753-37600464	1.72E-02	225	2119	-3.37	1.33E-04
IL1RN	2	113885138-113891592	1.74E-02	91	919	-3.42	1.37E-04
HIF1A	14	62162119-62214977	1.94E-02	901	8757	-3.26	1.54E-04
TMCC3	12	94960900-95044324	2.04E-02	35	419	-3.45	1.63E-04
CLESL1	4	185676749-185747215	2.04E-02	307	2990	-3.24	1.65E-04
CLEC5A	7	141627157-141646783	2.09E-02	20	321	-3.36	1.70E-04
SLC2A5	1	9097007-9129887	2.38E-02	3	140	-3.99	1.98E-04
SLC2A3	12	8071825-8088892	2.49E-02	1612	15486	-3.26	2.11E-04
ANGPTL4	19	8429011-8439257	2.69E-02	0	66	-3.90	2.30E-04
MXD1	2	70142203-70170074	2.93E-02	523	4746	-3.15	2.54E-04
NLRP3	1	247581351-247612404	2.93E-02	203	1914	-3.15	2.58E-04
RBM8A	1	145507638-145511444	2.93E-02	84	1055	-4.26	2.60E-04
SAT1	X	23801275-23804325	2.93E-02	3346	26184	-3.24	2.56E-04
DNTT	10	98064085-98098319	3.44E-02	7	178	-4.04	3.09E-04
NUCB2	11	17298286-17353069	3.44E-02	474	4708	-3.44	3.10E-04
VSTM1	19	54544085-54567207	3.68E-02	12	233	-3.53	3.35E-04
PHACTR1	6	12717833-13287528	4.00E-02	3	107	-3.34	3.67E-04
PADI4	1	17634690-17690495	4.02E-02	267	2607	-3.34	3.72E-04
NR4A1	12	52445191-52453285	4.22E-02	85	820	-3.07	3.97E-04
SERPINB10	18	61582745-61602474	4.23E-02	34	448	-3.50	4.01E-04
COL17A1	10	105791048-105845638	4.35E-02	5	154	-3.94	4.16E-04
CCL2	17	32582296-32584218	4.36E-02	6	141	-3.26	4.23E-04
CD93	20	23059994-23066977	4.36E-02	179	1456	-3.05	4.27E-04
CXCL16	17	4636830-4643223	4.36E-02	289	2143	-3.20	4.28E-04
DEFA5	8	6912829-6914259	4.36E-02	0	60	-3.78	4.31E-04
RLPL2	12	123899936-123921264	4.36E-02	281	2174	-3.06	4.33E-04
ARG1	6	131894365-131905468	4.67E-02	113	1060	-3.08	4.68E-04
CXCL12	10	44865607-44880545	4.72E-02	6	161	-3.54	4.77E-04

