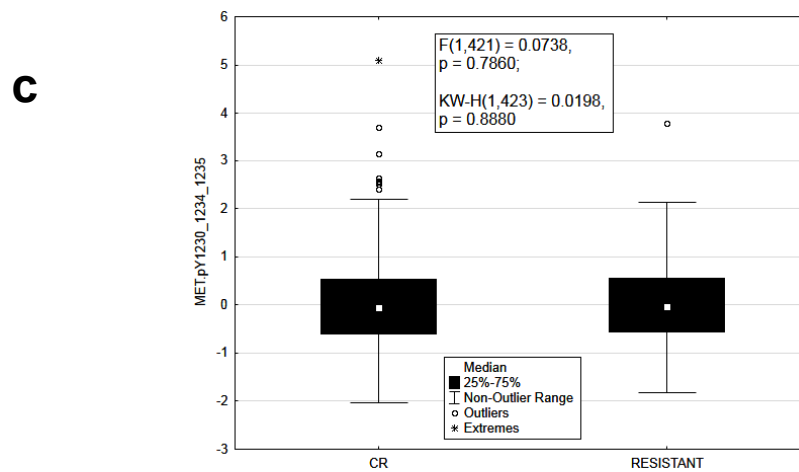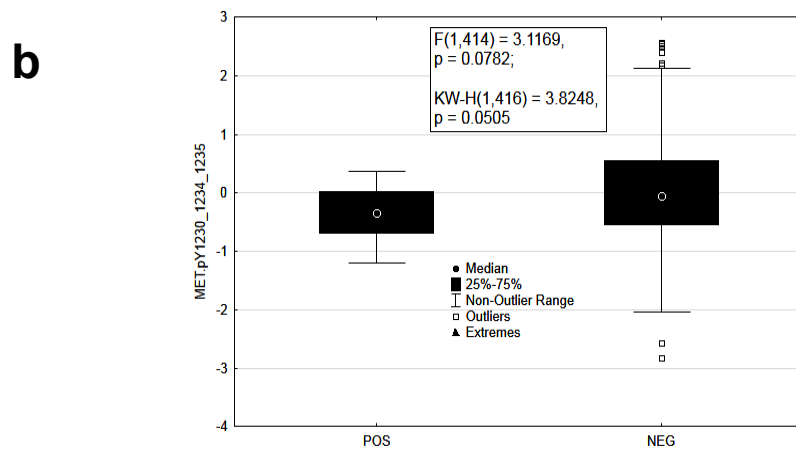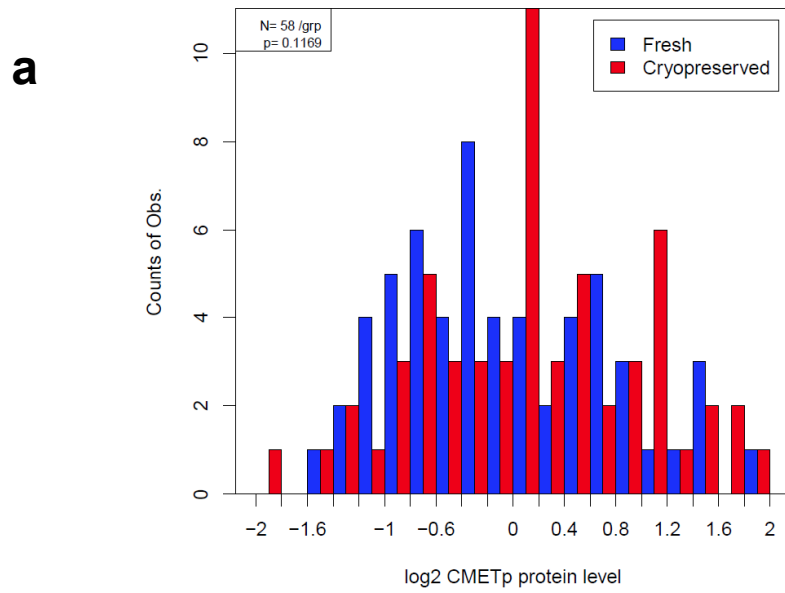**Supplementary Material**

McGee et al. Biological properties of ligand-dependent activation of the MET receptor kinase in acute myeloid leukemia.

Supplementary Figure 1

a

b

c

Supplementary Figure 1. (a) Distribution of protein levels for pairs of fresh and cryo-preserved samples showing no statistically significant difference in MET phosphorylation between the two sample types. **(b)** Analysis of MET phosphorylation as a function of FLT3 mutational status demonstrating an association of increased levels of MET phosphorylation in AML cells lacking FLT3 mutations. **(c)** Analysis of MET phosphorylation as a function of treatment response, demonstrating no apparent association with primary chemoresistance.
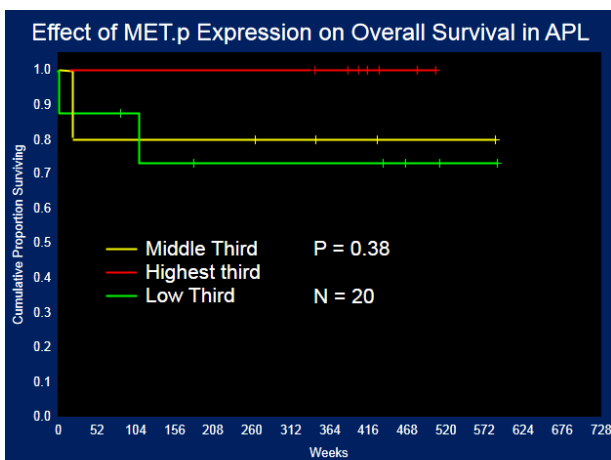
Supplementary Figure 2

a

	N	Events	Median	95% LCL	95% UCL	Logrank.p	Cox.p
Overall Survival	256	193	47.6	37.9	58.4	0.545	0.338
Event Free	205	170	23.6	18.9	32.0	0.353	0.131
CR Duration	123	74	54.7	42.4	97.9	0.026	0.272

b

Dependent Variable: New OS (AML & Nl B&M combo- 231AB-April 2014-METp analysis.sta)
Censoring var.: vital.status NEW
Chi² = 202.609 df = 6 p = 0.0000
Include condition: v3='aml' and v9='N'
Exclude condition: v46='na'

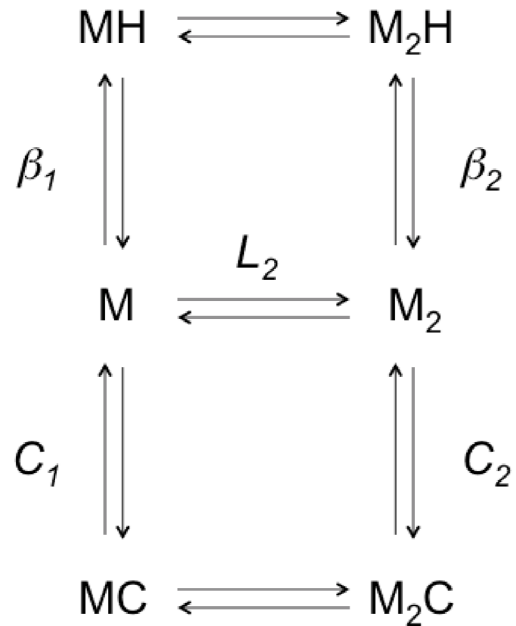| N=415	Beta	Standard Error	Beta 95% lower	Beta 95% upper	t-value	Wald Statist.	p	Risk ratio	Risk ratio 95% lower	Risk ratio 95% upper
Age.at.Dx	0.043400	0.004820	0.03395	0.052846	9.00469	81.08443	0.000000	1.044356	1.034536	1.054268
Performance.Status	0.341491	0.065161	0.21378	0.469205	5.24070	27.46488	0.000000	1.407044	1.238346	1.598722
WBC	0.006444	0.001202	0.00409	0.008800	5.35944	28.72360	0.000000	1.006464	1.004096	1.008839
Male	-0.317299	0.114582	-0.54188	-0.092723	-2.76920	7.66845	0.005623	0.728113	0.581656	0.911446
FavCyto	-0.902302	0.333517	-1.55598	-0.248621	-2.70542	7.31927	0.006826	0.405635	0.210982	0.779876
Unfavcyto	0.505975	0.112768	0.28495	0.726996	4.48688	20.13211	0.000007	1.658602	1.329702	2.068856

c

d
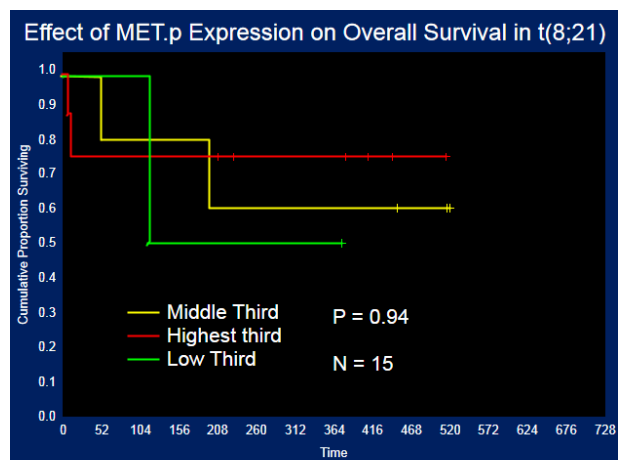
Supplementary Figure 2. (a) Summary of statistics from outcome analyses with survival reported in weeks. **(b)** Multivariate analysis of MET phosphorylation and overall survival. Kaplan-Meier analysis of overall survival in **(c)** APL (t(15;17)) and **(d)** AML1-ETO (t(18;21)) subgroups showing no association with MET activation.
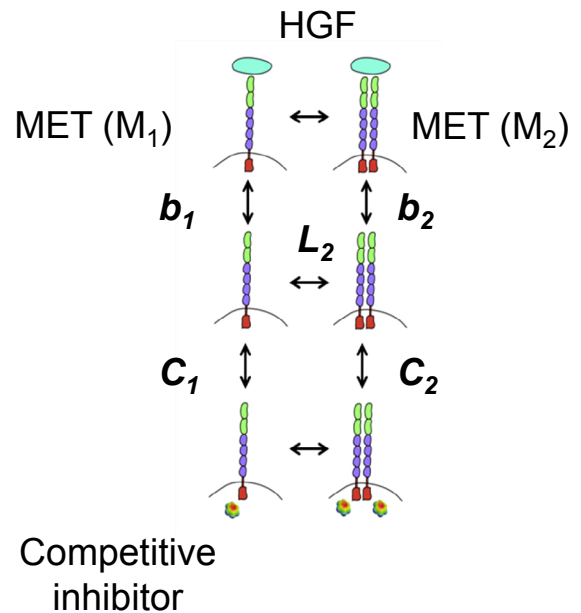
Supplemental Figure 3

a

Negatively Correlated	Positively Correlated
PTPN11	BAD.pS112
GSKA_B	RPS6KB1
MAPK1	CASP9.Cl330
GAPDH	PPARA
EIF4E	HDAC3
PARK7	BMI1
EIF2AK2	ZNF346
NCL	EGFR
PTEN	JUNB
EIF2S1	CASP9.cl315
HNRNPK	IRS1.pS1101
TSC2	BAK1
CASP3	PLAC1
PSMD9.pS10	CTSG
BRAF	YAP1p
MAP2K1	YWHAZ
MAPK9	NRP1
PA2G4	CDKN1A
INPP5D	IGFBP2
INPPL1	STAT1-pY701
MAPK14	NF2.pS518
STMN1	CTNNA1
XIAP	AKT1_2_3.pT308
SMAD2	CCND1
SIRT1	ODC1
SMAD3	ERBB3
KDR	GATA3
STK11	CTNNB1.pS33_37_
SMAD4	41
SMAD1	MSI2
BID	BIRC2
RELA	ATF3
	NOTCH3
	BIRC5
	RAC1_2_3

b

c

HGF

MET (M_1)   MET (M_2)

b_1 L_2 b_2

C_1 C_2

Competitive inhibitor

Supplementary Figure 3. (a) Proteins found by RPPA analysis to be positively and negatively associated with MET activation with Pearson correlation coefficients of > 0.2 and < -0.2, respectively. **(b)** Thermodynamic model of the interaction between ligand-dependent MET receptor activation and competitive MET kinase inhibition where (M) represents the MET receptor, (H) represents the HGF ligand, and (C) represents a competitive kinase inhibitor. **(c)** Illustration of the thermodynamic model of ligand-dependent MET receptor activation.