

Supplementary Material

Supplementary Tables

Table S1. Combination index analysis of TP53-wt AML cells

TP53-wt AML cell lines	Drug concentration [ $\mu$ M]		24h			48h			72h		
			WIP1i								
			5	10	20	5	10	20	5	10	20
MOLM-13	Nut-3a	0.5	0.24	0.25	0.33	0.79	0.83	0.85	0.84	0.85	0.88
		1	0.35	0.47	0.60	0.90	0.92	0.93	0.93	0.94	0.95
		2.5	0.72	0.70	0.77	0.95	0.96	0.97	0.96	0.98	0.98
		5	0.81	0.79	0.84	0.99	0.99	0.99	0.98	0.98	0.98
MV-4-11		0.5	0.23	0.33	0.29	0.22	0.18	0.16	0.44	0.54	0.60
		1	0.24	0.26	0.29	0.25	0.24	0.19	0.70	0.80	0.88
		2.5	0.41	0.51	0.48	0.39	0.47	0.30	1.28	1.36	1.50
		5	0.29	0.63	0.67	0.45	0.45	0.45	2.11	2.17	2.30
OCI-AML3		0.5	0.06	0.08	0.33	0.30	0.25	0.66	0.87	0.77	4.88
		1	0.90	0.09	0.11	0.26	0.25	0.28	0.91	1.90	3.21
		2.5	0.11	0.15	0.09	0.38	0.35	0.31	0.86	1.25	0.92
		5	0.10	0.08	0.04	0.34	0.34	0.31	0.79	0.98	0.89

Table S2. Characteristics of primary AML samples

Sample ID	Specimen Type	Karyotype	FLT3	NPM1	TP53
#1	PB	NA	ITD	mut	wt
#2	BM	48, XY, +6, +15 [30]	wt	wt	wt
#3	PB	46 XY [20]	ITD	mut	wt
#4	BM	NA	wt	wt	wt
#5	BM	46 XX [15]	wt	wt	wt
#6	BM	46, XY [20]	ITD	mut	wt
#7	BM	46, XY [20]	ITD	mut	wt
#8	BM	46, XY, del(2)(p21), t(5;11)(q23;q24) [20]	TKD	wt	wt
#9	BM	46, XX [15]	ITD	mut	wt
#10	BM	Complex	ITD	wt	wt
#11	BM	Complex	wt	wt	mut
#12	PB	Complex	wt	wt	mut
#13	BM	NA	wt	wt	mut

BM: bone marrow; ITD: internal tandem duplication; mut: mutated; NA: not available; PB: peripheral blood; TKD: mutated in the tyrosine kinase domain; wt: wildtype

**Table S3.** Top 20 upregulated (red) and downregulated (blue) genes in MV-4-11 cells treated with Nut-3a+WIP1i vs. control

Gene	Description	Chromosome	Fold change	p value
<i>MDM2</i>	MDM2 Proto-Oncogene, E3 Ubiquitin Protein Ligase	chr12	17.03	0.003
<i>TP53INP1</i>	Tumor Protein P53 Inducible Nuclear Protein 1	chr8	5.70	0.008
<i>XPC</i>	Xeroderma Pigmentosum, Complementation Group C	chr3	4.86	0.019
<i>ZMAT3</i>	Zinc Finger, Matrin-Type 3	chr3	4.66	0.001
<i>CDKN1A</i>	Cyclin-Dependent Kinase Inhibitor 1A (P21, Cip1)	chr6	3.68	0.038
<i>TOM1L1</i>	Target Of Myb1 Like 1 Membrane Trafficking Protein	chr17	2.87	0.014
<i>DYRK1B</i>	Dual Specificity Tyrosine-(Y)-Phosphorylation Regulated Kinase 1B	chr19	2.69	0.036
<i>MEI4</i>	Meiotic Double-Stranded Break Formation Protein 4	chr6	2.53	0.001
<i>SUMO4</i>	Small Ubiquitin-Like Modifier 4	chr6	2.43	0.045
<i>B3GAT1</i>	Beta-1,3-Glucuronyltransferase 1	chr11	2.41	0.024
<i>COL2A1</i>	Collagen, Type II, Alpha 1	chr12	2.35	0.003
<i>IRAK1BP1</i>	Interleukin 1 Receptor Associated Kinase 1 Binding Protein 1	chr6	2.35	0.015
<i>ALDH1A2</i>	Aldehyde Dehydrogenase 1 Family, Member A2	chr15	2.20	0.025
<i>ITGAD</i>	Integrin Alpha D	chr16	2.13	0.032
<i>HLA-A</i>	Major Histocompatibility Complex, Class I, A	chr6	2.11	0.048
<i>PROM1</i>	Prominin 1	chr4	2.10	0.015
<i>SIM1</i>	Single-Minded Family Bhlh Transcription Factor 1	chr6	2.08	0.014
<i>NAPSA</i>	Napsin A Aspartic Peptidase	chr19	2.07	0.011
<i>CYSRT1</i>	Cysteine-Rich Tail Protein 1	chr9	2.07	0.039
<i>NBR1</i>	Neighbor Of BRCA1 Gene 1	chr17	2.03	0.020
<i>HSPA14</i>	Heat Shock 70kda Protein 14	chr10	0.28	0.002
<i>UNG</i>	Uracil DNA Glycosylase	chr12	0.30	0.039
<i>RGSL1</i>	Regulator Of G-Protein Signaling Like 1	chr1	0.35	0.038
<i>FRMD3</i>	FERM Domain Containing 3	chr9	0.35	0.002
<i>ABHD17C</i>	Abhydrolase Domain Containing 17C	chr15	0.35	0.018
<i>TIMELESS</i>	Timeless Circadian Clock	chr12	0.36	0.042
<i>BCAT1</i>	Branched Chain Amino-Acid Transaminase 1, Cytosolic	chr12	0.36	0.014
<i>ARPC1A</i>	Actin Related Protein 2/3 Complex Subunit 1A	chr7	0.36	0.003
<i>PSMG4</i>	Proteasome (Prosome, Macropain) Assembly Chaperone 4	chr6	0.37	0.021
<i>RRM2</i>	Ribonucleotide Reductase M2	chr2	0.37	0.049
<i>HELLS</i>	Helicase, Lymphoid-Specific	chr10	0.39	0.027
<i>LBR</i>	Lamin B Receptor	chr1	0.40	0.031
<i>GSTA2</i>	Glutathione S-Transferase Alpha 2	chr6	0.40	0.025
<i>SLC27A2</i>	Solute Carrier Family 27 (Fatty Acid Transporter), Member 2	chr15	0.41	0.018

<i>ICAM3</i>	Intercellular Adhesion Molecule 3	chr19	0.42	0.006
<i>DCUN1D5</i>	DCN1, Defective In Cullin Neddylation 1, Domain Containing 5	chr11	0.42	0.016
<i>SETD4</i>	SET Domain Containing 4	chr21	0.42	0.043
<i>SETD7</i>	SET Domain Containing (Lysine Methyltransferase) 7	chr4	0.43	0.008
<i>TREML2</i>	Triggering Receptor Expressed On Myeloid Cells-Like 2	chr6	0.43	0.032

**Table S4.** Top 20 upregulated (red) and downregulated (blue) genes in NOMO-1 cells treated with Nut3a+WIP1i vs. control

Gene	Description	Chromosome	Fold change	p value
<i>FABP4</i>	Fatty Acid Binding Protein 4, Adipocyte	chr8	45.25	0.003
<i>CD36</i>	Cd36 Molecule (Thrombospondin Receptor)	chr7	36.76	0.016
<i>LACC1</i>	Laccase (Multicopper Oxidoreductase) Domain 1	chr13	20.39	0.015
<i>SLC39A8</i>	Solute Carrier Family 39 (Zinc Transporter), Member 8	chr4	14.83	0.033
<i>TNFRSF9</i>	Tumor Necrosis Factor Receptor Superfamily, Member 9	chr1	8.28	0.003
<i>ME1</i>	Malic Enzyme 1, NADP(+)-Dependent, Cytosolic	chr6	5.98	0.015
<i>PLIN2</i>	Perilipin 2	chr9	5.98	0.019
<i>CCL18</i>	Chemokine (C-C Motif) Ligand 18	chr17	5.24	0.024
<i>IER3</i>	Immediate Early Response 3	chr6	5.21	0.038
<i>G0S2</i>	G0/G1 Switch 2	chr1	4.89	0.006
<i>GPR84</i>	G Protein-Coupled Receptor 84	chr12	4.50	0.005
<i>LPAR6</i>	Lysophosphatidic Acid Receptor 6	chr13	4.23	0.012
<i>ZFP36L1</i>	Zfp36 Ring Finger Protein-Like 1	chr14	3.97	0.020
<i>IL7R</i>	Interleukin 7 Receptor	chr5	3.94	0.042
<i>PHLDA1</i>	Pleckstrin Homology-Like Domain, Family A, Member 1	chr12	3.92	0.007
<i>SOD2</i>	Superoxide Dismutase 2, Mitochondrial	chr6	3.92	0.042
<i>PDK4</i>	Pyruvate Dehydrogenase Kinase, Isozyme 4	chr7	3.86	0.044
<i>ALDH1L2</i>	Aldehyde Dehydrogenase 1 Family, Member L2	chr12	3.81	0.008
<i>LDHAL6B</i>	Lactate Dehydrogenase A-Like 6b	chr15	3.34	0.022
<i>TRPV5</i>	Transient Receptor Potential Cation Channel Subfamily V, Member 5	chr7	3.10	0.033
<i>STK25</i>	Serine/Threonine Kinase 25	chr2	0.37	0.022
<i>NEIL3</i>	Nei-Like Dna Glycosylase 3	chr4	0.37	0.041
<i>CDCA5</i>	Cell Division Cycle Associated 5	chr11	0.37	0.039
<i>TMEM55B</i>	Transmembrane Protein 55b	chr14	0.37	≤0.001
<i>DUS2</i>	Dihydrouridine Synthase 2	chr16	0.37	0.010
<i>PYCR1</i>	Pyrroline-5-Carboxylate Reductase 1	chr17	0.37	0.034
<i>LASP1</i>	Lim And Sh3 Protein 1	chr17	0.38	0.042
<i>PAK1</i>	P21 Protein (Cdc42/Rac)-Activated Kinase 1	chr11	0.38	0.047
<i>DEFB1</i>	Defensin, Beta 1	chr8	0.38	0.023
<i>PPP2R5D</i>	Protein Phosphatase 2, Regulatory Subunit B, Delta	chr6	0.38	0.025
<i>INPP5D</i>	Inositol Polyphosphate-5-Phosphatase D	chr12	0.38	0.020

<i>ZNF692</i>	Zinc Finger Protein 692	chr1	0.38	0.040
<i>HHIP</i>	Hedgehog Interacting Protein	chr4	0.38	0.029
<i>DTYMK</i>	Deoxythymidylate Kinase	chr2	0.38	0.009
<i>UBXN11</i>	Ubx Domain Protein 11	chr1	0.38	0.050
<i>PBX2</i>	Pre-B-Cell Leukemia Homeobox 2	chr6	0.38	0.006
<i>CDCA2</i>	Cell Division Cycle Associated 2	chr8	0.38	0.039
<i>MAP4K2</i>	Mitogen-Activated Protein Kinase Kinase Kinase Kinase 2	chr11	0.38	0.016
<i>ANXA8</i>	Annexin A8	chr10	0.39	0.019
<i>ANAPC4</i>	Anaphase Promoting Complex Subunit 4	chr4	0.39	0.017

**Table S5.** Top 20 upregulated (red) and downregulated (blue) genes in MV-4-11 cells treated with Nut3a+WIP1i *vs.* WIP1i

Gene	Description	Chromosome	Fold change	p value
<i>MDM2</i>	MDM2 Proto-Oncogene, E3 Ubiquitin Protein Ligase	chr12	17.03	0.002
<i>TP53INP1</i>	Tumor Protein P53 Inducible Nuclear Protein 1	chr8	5.70	0.008
<i>XPC</i>	Xeroderma Pigmentosum, Complementation Group C	chr3	4.86	0.019
<i>ZMAT3</i>	Zinc Finger, Matrin-Type 3	chr3	4.66	≤0.001
<i>CDKN1A</i>	Cyclin-Dependent Kinase Inhibitor 1A (P21, Cip1)	chr6	3.68	0.038
<i>TOM1L1</i>	Target Of Myb1 Like 1 Membrane Trafficking Protein	chr17	2.87	0.013
<i>DYRK1B</i>	Dual Specificity Tyrosine-(Y)-Phosphorylation Regulated Kinase 1B	chr19	2.69	0.036
<i>MEI4</i>	Meiotic Double-Stranded Break Formation Protein 4	chr6	2.53	≤0.001
<i>SUMO4</i>	Small Ubiquitin-Like Modifier 4	chr6	2.43	0.045
<i>B3GAT1</i>	Beta-1,3-Glucuronyltransferase 1	chr11	2.41	0.024
<i>COL2A1</i>	Collagen, Type II, Alpha 1	chr12	2.35	0.003
<i>IRAK1BP1</i>	Interleukin 1 Receptor Associated Kinase 1 Binding Protein 1	chr6	2.35	0.015
<i>ALDH1A2</i>	Aldehyde Dehydrogenase 1 Family, Member A2	chr15	2.20	0.025
<i>ITGAD</i>	Integrin Alpha D	chr16	2.13	0.031
<i>HLA-A</i>	Major Histocompatibility Complex, Class I, A	chr6	2.11	0.047
<i>PROM1</i>	Prominin 1	chr4	2.10	0.014
<i>SIM1</i>	Single-Minded Family Bhlh Transcription Factor 1	chr6	2.08	0.014
<i>NAPSA</i>	Napsin A Aspartic Peptidase	chr19	2.07	0.010
<i>CYSRT1</i>	Cysteine-Rich Tail Protein 1	chr9	2.07	0.039
<i>NBR1</i>	Neighbor Of BRCA1 Gene 1	chr17	2.03	0.019
<i>HSPA14</i>	Heat Shock 70kda Protein 14	chr10	0.28	0.001
<i>UNG</i>	Uracil DNA Glycosylase	chr12	0.30	0.038
<i>RGSL1</i>	Regulator Of G-Protein Signaling Like 1	chr1	0.35	0.038
<i>FRMD3</i>	FERM Domain Containing 3	chr9	0.35	0.001
<i>ABHD17C</i>	Abhydrolase Domain Containing 17C	chr15	0.35	0.018
<i>TIMELESS</i>	Timeless Circadian Clock	chr12	0.36	0.041
<i>BCAT1</i>	Branched Chain Amino-Acid Transaminase 1, Cytosolic	chr12	0.36	0.014
<i>ARPC1A</i>	Actin Related Protein 2/3 Complex Subunit 1A	chr7	0.36	0.003
<i>PSMG4</i>	Proteasome (Prosome, Macropain) Assembly Chaperone 4	chr6	0.37	0.020
<i>RRM2</i>	Ribonucleotide Reductase M2	chr2	0.37	0.048
<i>HELLS</i>	Helicase, Lymphoid-Specific	chr10	0.39	0.026

<i>LBR</i>	Lamin B Receptor	chr1	0.40	0.030
<i>GSTA2</i>	Glutathione S-Transferase Alpha 2	chr6	0.40	0.025
<i>SLC27A2</i>	Solute Carrier Family 27 (Fatty Acid Transporter), Member 2	chr15	0.41	0.017
<i>ICAM3</i>	Intercellular Adhesion Molecule 3	chr19	0.42	0.006
<i>DCUN1D5</i>	DCN1, Defective In Cullin Neddylation 1, Domain Containing 5	chr11	0.42	0.016
<i>SETD4</i>	SET Domain Containing 4	chr21	0.42	0.043
<i>SETD7</i>	SET Domain Containing (Lysine Methyltransferase) 7	chr4	0.43	0.007
<i>TREML2</i>	Triggering Receptor Expressed On Myeloid Cells-Like 2	chr6	0.43	0.031

**Table S6.** Top 20 upregulated (red) and downregulated (blue) genes in NOMO-1 cells treated with Nut3a+WIP1i *vs.* WIP1i

Gene	Description	Chromosome	Fold change	p value
<i>CCL3</i>	Chemokine (C-C Motif) Ligand 3	chr17	13.93	0.032
<i>LACC1</i>	Laccase (Multicopper Oxidoreductase) Domain Containing 1	chr13	11.00	0.024
<i>TNFRSF9</i>	Tumor Necrosis Factor Receptor Superfamily, Member 9	chr1	8.40	0.002
<i>GPR84</i>	G Protein-Coupled Receptor 84	chr12	8.34	0.015
<i>G0S2</i>	G0/G1 Switch 2	chr1	5.35	0.003
<i>RGL1</i>	Ral Guanine Nucleotide Dissociation Stimulator-Like 1	chr1	5.31	0.026
<i>SOD2</i>	Superoxide Dismutase 2, Mitochondrial	chr6	4.29	0.033
<i>RASGRP1</i>	Ras Guanyl Releasing Protein 1	chr15	3.97	0.038
<i>ZFP36L1</i>	Zfp36 Ring Finger Protein-Like 1	chr14	3.61	0.003
<i>CALCOCO1</i>	Calcium Binding And Coiled-Coil Domain 1	chr12	3.32	0.003
<i>ARL4C</i>	Adp-Ribosylation Factor Like Gtpase 4c	chr2	3.14	0.043
<i>ME1</i>	Malic Enzyme 1, Nadp(+)-Dependent, Cytosolic	chr6	3.01	0.036
<i>DUSP16</i>	Dual Specificity Phosphatase 16	chr12	2.99	0.014
<i>ADGRE1</i>	Adhesion G Protein-Coupled Receptor E1	chr19	2.99	0.022
<i>GPR132</i>	G Protein-Coupled Receptor 132	chr14	2.71	0.029
<i>PLA2G7</i>	Phospholipase A2, Group Vii	chr6	2.66	0.028
<i>TNFSF15</i>	Tumor Necrosis Factor (Ligand) Superfamily, Member 15	chr9	2.64	0.021
<i>FABP6</i>	Fatty Acid Binding Protein 6, Ileal	chr5	2.64	0.009
<i>NFAT5</i>	Nuclear Factor Of Activated T-Cells 5, Tonicity-Responsive	chr16	2.60	0.049
<i>COX7A1</i>	Cytochrome C Oxidase Subunit Vii Polypeptide 1	chr19	2.60	0.044
<i>ADGRA3</i>	Adhesion G Protein-Coupled Receptor A3	chr4	0.17	0.049
<i>KCNQ5</i>	Potassium Channel, Voltage Gated Kqt-Like Subfamily Q, Member 5	chr6	0.17	0.039
<i>MARC1</i>	Mitochondrial Amidoxime Reducing Component 1	chr1	0.20	0.036
<i>CEP70</i>	Centrosomal Protein 70kda	chr3	0.21	0.042
<i>CA2</i>	Carbonic Anhydrase Ii	chr8	0.22	0.018
<i>SGTA</i>	Small Glutamine-Rich Tetratricopeptide Repeat (Tpr)-Containing, Alpha	chr19	0.24	0.045
<i>BCAP29</i>	B-Cell Receptor-Associated Protein 29	chr7	0.24	0.023
<i>SDHAF3</i>	Succinate Dehydrogenase Complex Assembly Factor 3	chr7	0.25	0.008
<i>IKBKAP</i>	Inhibitor Of Kappa Light Polypeptide Gene Enhancer In B-Cells, Kinase Complex-Associated Protein	chr9	0.26	0.025
<i>CR1</i>	Complement Component (3b/4b) Receptor 1	chr1	0.30	0.041
<i>DTD1</i>	D-Tyrosyl-Trna Deacylase 1	chr20	0.30	0.038

<i>FANCG</i>	Fanconi Anemia Complementation Group G	chr9	0.30	0.001
<i>HIST2H4A;</i> <i>HIST2H4B</i>	Histone Cluster 2, H4a; Histone Cluster 2, H4b	chr1	0.30	0.011
<i>PELP1</i>	Proline, Glutamate And Leucine Rich Protein 1	chr17	0.31	0.021
<i>NCK2</i>	Nck Adaptor Protein 2	chr2	0.32	0.038
<i>HIST2H4B;</i> <i>HIST2H4A</i>	Histone Cluster 2, H4b; Histone Cluster 2, H4a	chr1	0.32	0.025
<i>MRPL14</i>	Mitochondrial Ribosomal Protein L14	chr6	0.33	0.045
<i>COLGALT1</i>	Collagen Beta(1-O)Galactosyltransferase 1	chr19	0.33	0.032
<i>HELLS</i>	Helicase, Lymphoid-Specific	chr10	0.33	0.047
<i>TNSF13B</i>	Tumor Necrosis Factor (ligand) Superfamily, Member 13B	chr13	0.33	0.048

**Table S7.** Top 20 upregulated (red) and downregulated (blue) genes in MV-4-11 cells treated with Nut3a+WIP1i vs. Nut-3a

Gene	Description	Chromosome	Fold change	p value
<i>MDM2</i>	MDM2 Proto-Oncogene, E3 Ubiquitin Protein Ligase	chr12	6.77	0.005
<i>MMP16</i>	Matrix Metallopeptidase 16 (Membrane-Inserted)	chr8	3.27	0.042
<i>SETBP1</i>	SET Binding Protein 1	chr18	2.91	0.023
<i>ZMAT3</i>	Zinc Finger, Matrin-Type 3	chr3	2.69	0.002
<i>ZBTB33</i>	Zinc Finger And BTB Domain Containing 33	chrX	2.60	0.017
<i>TMEM229B</i>	Transmembrane Protein 229B	chr14	2.39	0.001
<i>TIGAR</i>	TP53 Induced Glycolysis Regulatory Phosphatase	chr12	2.33	0.049
<i>COL2A1</i>	Collagen, Type II, Alpha 1	chr12	2.30	≤0.001
<i>GPA33</i>	Glycoprotein A33 (Transmembrane)	chr1	2.27	0.001
<i>VSIG10</i>	V-Set And Immunoglobulin Domain Containing 10	chr12	2.27	0.014
<i>ZFP90</i>	ZFP90 Zinc Finger Protein	chr16	2.25	0.044
<i>HERC6</i>	HECT And RLD Domain Containing E3 Ubiquitin Protein Ligase Family Member 6	chr4	2.23	0.021
<i>ZNF91</i>	Zinc Finger Protein 91	chr19	2.23	0.006
<i>CCDC188</i>	Coiled-Coil Domain Containing 188	chr22	2.20	0.043
<i>ZNF260</i>	Zinc Finger Protein 260	chr2	2.17	0.013
<i>FAM19A2</i>	Family With Sequence Similarity 19 (Chemokine (C-C Motif)-Like), Member A2	chr17	2.14	0.004
<i>HMX2</i>	H6 Family Homeobox 2	chr15	2.14	0.017
<i>ISG20</i>	Interferon Stimulated Exonuclease Gene 20kda	chr19	2.14	0.028
<i>ZNF404</i>	Zinc Finger Protein 404	chr12	2.14	0.002
<i>YPEL1</i>	Yippee Like 1	chr10	2.13	0.011
<i>FOXM1</i>	Forkhead Box M1	chr4	0.33	0.043
<i>YWHAH</i>	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein, Eta	chr16	0.34	0.021
<i>VAT1</i>	Vesicle Amine Transport 1	chr1	0.36	0.041
<i>AARS</i>	Alanyl-Trna Synthetase	chr5	0.36	0.023
<i>RARA</i>	Retinoic Acid Receptor, Alpha	chr1	0.38	0.024
<i>ORC1</i>	Origin Recognition Complex Subunit 1	chr19	0.38	0.008
<i>RNF145</i>	Ring Finger Protein 145	chr12	0.39	0.043
<i>RNF41</i>	Ring Finger Protein 41, E3 Ubiquitin Protein Ligase	chr16	0.40	0.012
<i>MCM6</i>	Minichromosome Maintenance Complex Component 6	chr17	0.40	0.016

<i>SPTBN1</i>	Spectrin, Beta, Non-Erythrocytic 1	chr11	0.40	0.025
<i>DNAAF1</i>	Dynein, Axonemal, Assembly Factor 1	chr1	0.40	0.034
<i>E2F8</i>	E2F Transcription Factor 8	chr12	0.41	0.047
<i>RNASE2</i>	Ribonuclease, Rnase A Family, 2 (Liver, Eosinophil-Derived Neurotoxin)	chr17	0.43	0.022
<i>SEN3</i>	SUMO1/Sentrin/SMT3 Specific Peptidase 3	chr11	0.43	0.050
<i>SMG6</i>	SMG6 Nonsense Mediated Mrna Decay Factor	chr21	0.43	0.038
<i>CDCA5</i>	Cell Division Cycle Associated 5	chr8	0.44	0.028
<i>CHAF1B</i>	Chromatin Assembly Factor 1, Subunit B (P60)	chr9	0.44	0.029
<i>CHRNE</i>	Cholinergic Receptor, Nicotinic Epsilon	chr3	0.44	0.021
<i>PLD1</i>	Phospholipase D1, Phosphatidylcholine-Specific	chr15	0.44	0.037
<i>USP17L2</i>	Ubiquitin Specific Peptidase 17-Like Family Member 2	chr11	0.44	0.035

**Table S8.** Top 20 upregulated (red) and downregulated (blue) genes in NOMO-1 cells treated with Nut3a+WIP1i vs. Nut-3a

Gene	Description	Chromosome	Fold change	p value
<i>FABP4</i>	Fatty Acid Binding Protein 4, Adipocyte	chr8	38.59	0.004
<i>CALCOCO1</i>	Calcium Binding And Coiled-Coil Domain 1	chr12	4.82	0.015
<i>ZNF518B</i>	Zinc Finger Protein 518B	chr4	4.53	0.019
<i>PHGDH</i>	Phosphoglycerate Dehydrogenase	chr1	4.47	0.050
<i>LY6G6C</i>	Lymphocyte Antigen 6 Complex, Locus G6C	chr6	4.06	0.050
<i>ME1</i>	Malic Enzyme 1, NADP(+)-Dependent, Cytosolic	chr6	3.61	0.024
<i>ANXA5</i>	Annexin A5	chr4	3.12	0.042
<i>FAM219A</i>	Family With Sequence Similarity 219, Member A	chr9	3.05	0.013
<i>KCNAB1</i>	Potassium Channel, Voltage Gated Subfamily A Regulatory Beta Subunit 1	chr3	3.03	0.036
<i>IL23R</i>	Interleukin 23 Receptor	chr1	2.95	0.042
<i>STAC2</i>	SH3 And Cysteine Rich Domain 2	chr17	2.83	0.019
<i>C17orf99</i>	Chromosome 17 Open Reading Frame 99	chr17	2.71	0.049
<i>SMG5</i>	SMG5 Nonsense Mediated Mrna Decay Factor	chr1	2.69	0.024
<i>HEATR4</i>	HEAT Repeat Containing 4	chr14	2.69	0.046
<i>KMO</i>	Kynurenine 3-Monooxygenase (Kynurenine 3-Hydroxylase)	chr1	2.68	0.043
<i>UGT2B10</i>	UDP Glucuronosyltransferase 2 Family, Polypeptide B10	chr4	2.68	0.034
<i>TNFRSF9</i>	Tumor Necrosis Factor Receptor Superfamily, Member 9	chr1	2.62	0.028
<i>TNFSF4</i>	Tumor Necrosis Factor (Ligand) Superfamily, Member 4	chr1	2.53	0.001
<i>IGDCC3</i>	Immunoglobulin Superfamily, DCC Subclass, Member 3	chr15	2.53	0.049
<i>PRMT8</i>	Protein Arginine Methyltransferase 8	chr12	2.51	0.017
<i>PPP1R27</i>	Protein Phosphatase 1, Regulatory Subunit 27	chr17	0.08	0.048
<i>HIST2H4B;</i> <i>HIST2H4A</i>	Histone Cluster 2, H4b; Histone Cluster 2, H4a	chr1	0.08	0.033
<i>CTSG</i>	Cathepsin G	chr14	0.09	0.016
<i>IL18RAP</i>	Interleukin 18 Receptor Accessory Protein	chr2	0.12	0.016
<i>HIST1H3B</i>	Histone Cluster 1, H3b	chr6	0.15	0.048
<i>SPP1</i>	Secreted Phosphoprotein 1	chr4	0.16	0.042
<i>HIST1H2AK</i>	Histone Cluster 1, H2ak	chr6	0.17	0.012
<i>PDAP1</i>	PDGFA Associated Protein 1	chr7	0.17	0.045
<i>HIST1H2BI</i>	Histone Cluster 1, H2bi	chr6	0.18	0.041

<i>HIST2H3A</i>	Histone Cluster 2, H3a	chr1	0.18	0.012
<i>ATP5I</i>	ATP Synthase, H <sup>+</sup> Transporting, Mitochondrial Fo Complex Subunit E	chr4	0.20	0.036
<i>SLC6A8</i>	Solute Carrier Family 6, Member 8	chrX	0.21	0.018
<i>CLEC11A</i>	C-Type Lectin Domain Family 11, Member A	chr19	0.21	0.018
<i>RPS27A</i>	Ribosomal Protein S27a	chr2	0.21	0.043
<i>CCR2</i>	Chemokine (C-C Motif) Receptor 2	chr3	0.21	0.016
<i>INPP5K</i>	Inositol Polyphosphate-5-Phosphatase K	chr17	0.22	0.046
<i>PSMD8</i>	Proteasome 26S Subunit, Non-AtPase 8	chr19	0.22	0.036
<i>ART3</i>	ADP-Ribosyltransferase 3	chr4	0.23	0.011
<i>HIST1H2AE</i>	Histone Cluster 1, H2ae	chr6	0.23	0.048
<i>DEPDC1</i>	DEP Domain Containing 1	chr1	0.24	0.049

**Table S9.** P53 target\* and signature\*\* genes that are significantly upregulated in MV-4-11 or NOMO-1 cells treated with Nut-3a+WIP1i *vs.* control.

Gene	Description	Chromosome	Fold change	p value	Cell line
<i>MDM2</i>	MDM2 proto-oncogene, E3 ubiquitin protein ligase	chr12	40.50	0.002	MV-4-11
<i>CDKN1A</i>	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	chr6	12.73	0.012	MV-4-11
<i>TP53INP1</i>	tumor protein p53 inducible nuclear protein 1	chr8	12.73	0.006	MV-4-11
<i>EDA2R</i>	ectodysplasin A2 receptor	chrX	11.47	0.021	MV-4-11
<i>TIGAR</i>	TP53 induced glycolysis regulatory phosphatase	chr12	10.78	0.001	MV-4-11
<i>TRIM22</i>	UTR5 best transcript NM_001199573	chr11	10.48	0.004	MV-4-11
<i>XPC</i>	xeroderma pigmentosum, complementation group C	chr3	9.85	0.006	MV-4-11
<i>APOBEC3H</i>	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3H	chr22	7.94	0.038	MV-4-11
<i>SESN1</i>	sestrin 1	chr6	6.96	0.000	MV-4-11
<i>ZMAT3</i>	zinc finger, matrin-type 3	chr3	6.87	0.001	MV-4-11
<i>POLH</i>	polymerase (DNA directed), eta	chr6	5.82	0.025	MV-4-11
<i>FDXR</i>	ferredoxin reductase	chr17	5.06	0.006	MV-4-11
<i>MLF2</i>	myeloid leukemia factor 2	chr12	4.79	0.000	MV-4-11
<i>PLK2</i>	polo-like kinase 2	chr5	4.23	0.003	MV-4-11
<i>FBXO22</i>	F-box protein 22	chr15	4.11	0.031	MV-4-11
<i>CYFIP2</i>	cytoplasmic FMR1 interacting protein 2	chr5	3.92	0.034	MV-4-11
<i>ANXA4</i>	intronic best transcript NM_0011153	chr2	3.53	0.032	MV-4-11
<i>DCP1B</i>	decapping mRNA 1B	chr12	3.16	0.038	MV-4-11
<i>LAPTM5</i>	lysosomal protein transmembrane 5	chr1	3.12	0.046	MV-4-11
<i>DDB2</i>	damage-specific DNA binding protein 2	chr11	2.97	0.024	MV-4-11
<i>RETSAT</i>	retinol saturase (all-trans-retinol 13,14-reductase)	chr2	2.83	0.039	MV-4-11
<i>TNFSF9</i>	tumor necrosis factor (ligand) superfamily, member 9	chr19	2.83	0.003	MV-4-11

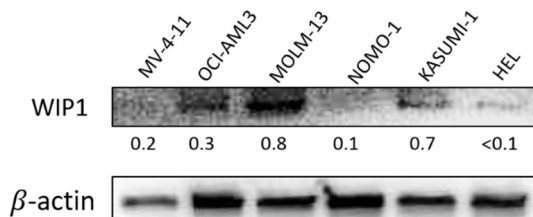


<i>MRPL49</i>	mitochondrial ribosomal protein L49	chr11	2.79	0.017	MV-4-11
<i>DOCK8</i>	dedicator of cytokinesis 8	chr9	2.77	0.037	MV-4-11
<i>TNFRSF10C</i>	tumor necrosis factor receptor superfamily, member 10c, decoy without an intracellular domain	chr8	2.55	0.002	MV-4-11
<i>FBXO32</i>	F-box protein 32	chr8	2.36	0.036	MV-4-11
<i>ISCU</i>	iron-sulfur cluster assembly enzyme	chr12	2.36	0.011	MV-4-11
<i>MR1</i>	major histocompatibility complex, class I-related	chr1	2.25	0.012	MV-4-11
<i>IER5</i>	immediate early response 5	chr1	2.17	0.013	MV-4-11
<i>ZNF195</i>	zinc finger protein 195	chr11	2.13	0.021	MV-4-11
<i>BTBD10</i>	BTB (POZ) domain containing 10	chr11	2.10	0.021	MV-4-11
<i>HHAT</i>	hedgehog acyltransferase		2.07	0.010	MV-4-11
<i>GADD45A</i>	growth arrest and DNA-damage-inducible, alpha	chr1	2.06	0.013	MV-4-11
<i>NINJ1</i>	ninjurin 1	chr9	2.17	0.012	NOMO-1
<i>LACCI1</i>	laccase (multicopper oxidoreductase) domain containing 1	chr13	20.39	0.015	NOMO-1
<i>VWCE</i>	von Willebrand factor C and EGF domains	chr11	2.10	0.007	NOMO-1

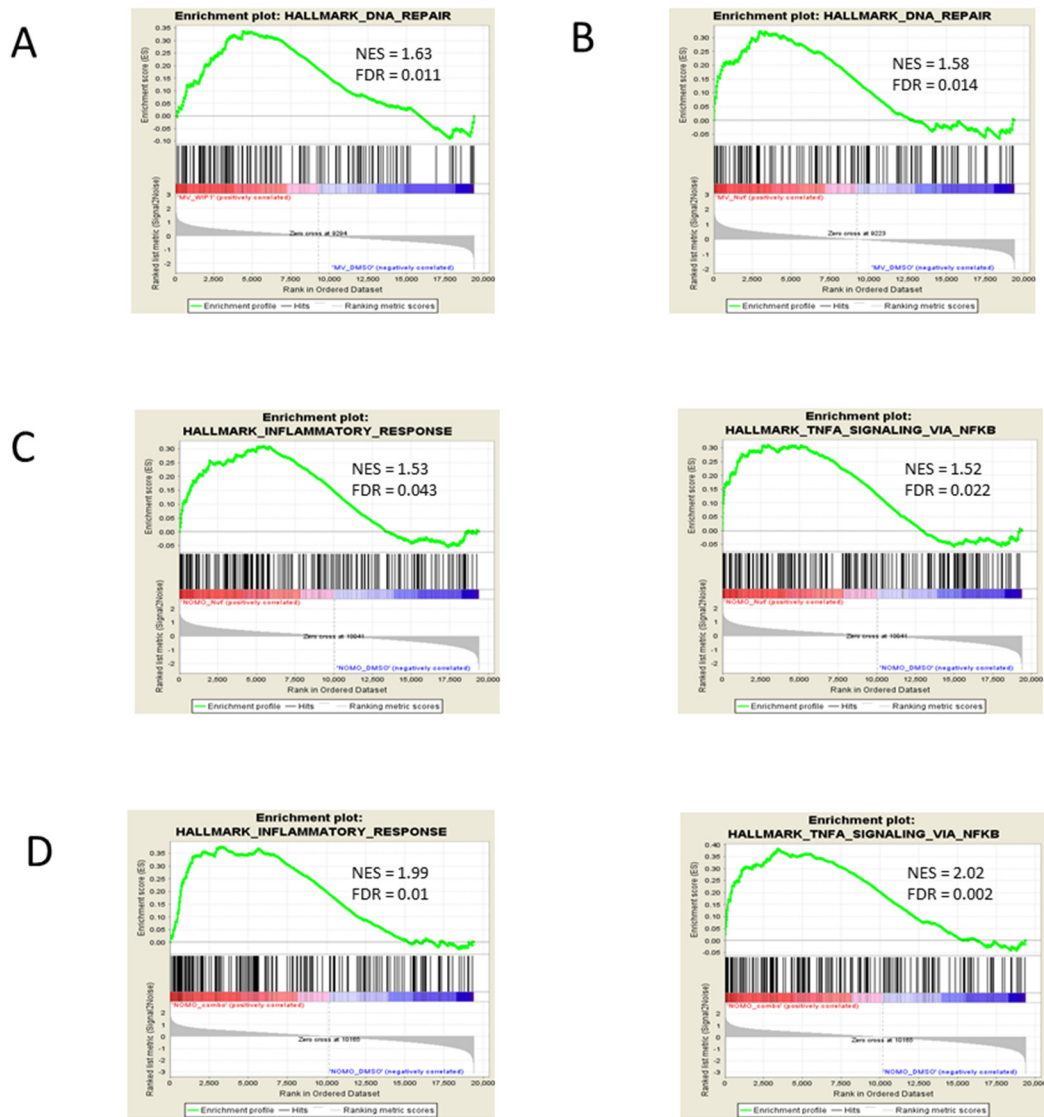
\* p53 targets from Fischer M, *Oncogene* 2017.

\*\* genes from the "Hallmark p53 pathway" MSigDB signature.

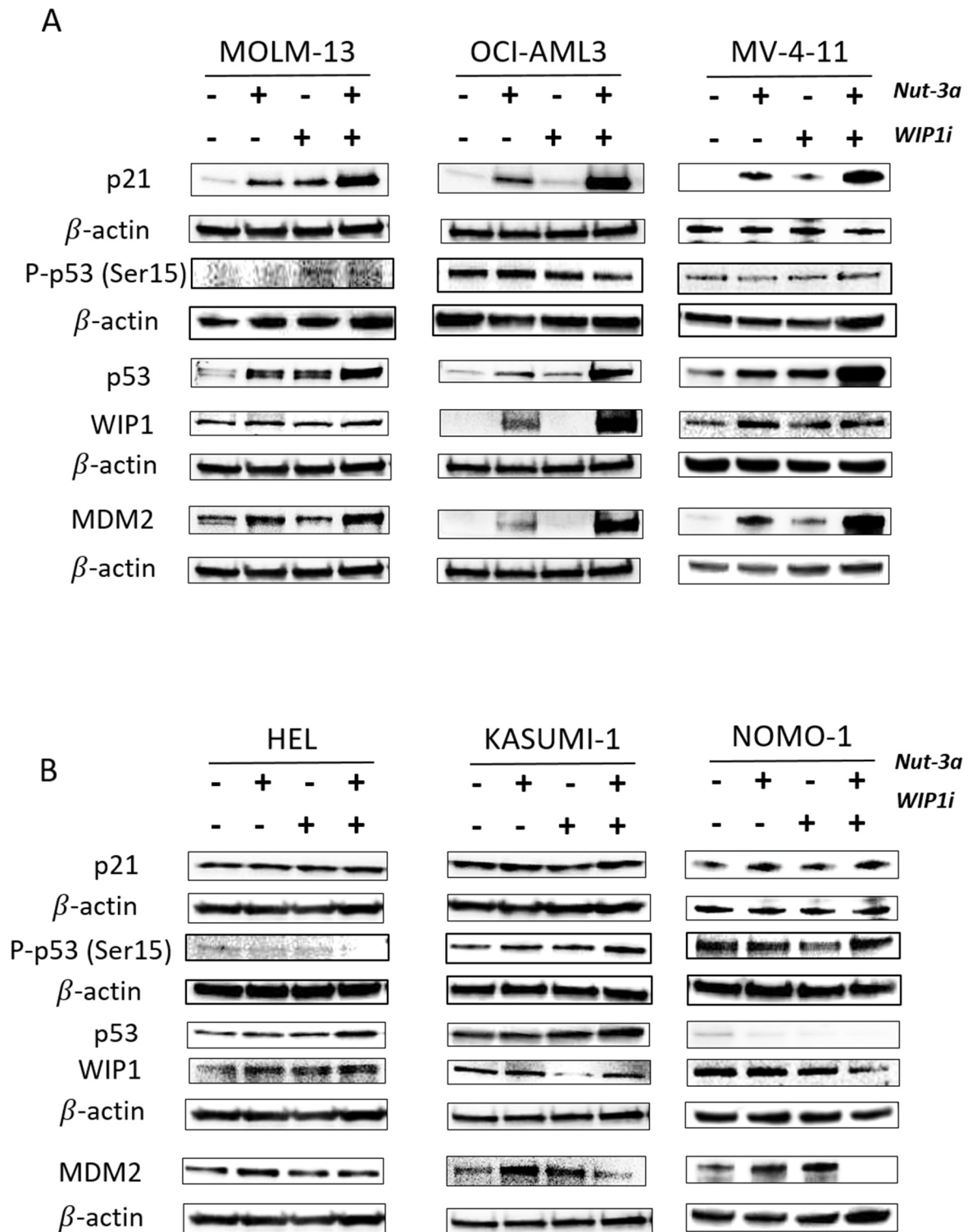
### Supplementary Figures



**Figure S1. WIP1 protein expression in AML cell lines.** Representative western blot of WIP1 expression in *TP53*-wt (MV-4-11, OCI-AML3, MOLM-13) and *TP53*-mut (NOMO-1, KASUMI-1, HEL) cell lines. Values indicate WIP1 expression normalized on  $\beta$ -actin.



**Figure S2. Additional transcriptional signatures in single and combined-treatment enriched in MV-4-11 and NOMO-1 cells.** GSEA plots of MV-4-11 cells treated with (A) WIP1i *vs.* DMSO, (B) Nut-3a *vs.* DMSO. GSEA common plots of NOMO-1 cells treated with (C) Nut-3a *vs.* DMSO, (D) Nut-3a+WIP1i *vs.* DMSO.



**Figure S3. Expression changes of p53 and its related genes induced by the treatment in *TP53*-wt and *TP53*-mut cells.** Representative western blots of p53-related genes in (A) MOLM-13, OCI-AML3 and MV-4-11 and (B) HEL, KASUMI-1 and NOMO-1 cells after 16h of treatment (*Nut-3a* 0.5, 2.5 and 0.5  $\mu$ M; *WIP1i* 10, 20, 5  $\mu$ M respectively for *TP53*-wt cells; *Nut-3a* 5  $\mu$ M and *WIP1i* 20  $\mu$ M for all the *TP53*-mut cells).