

Supplemental Table 1. Common genes that are both significantly differentially expressed between patients with MDM2+ and MDM2– DLBCL with WT-p53 (*P* value cutoff: .0012, false discovery rate for multiple t-tests: .30), and between patients with MDM2+ and MDM2– DLBCL with MUT-p53 (*P* value cutoff: .0023, false discovery rate: .30). The major gene function is according to the UniProt Knowledgebase (<http://www.uniprot.org>).

(1) Significantly upregulated genes in MDM2+ DLBCLs with WT-p53 or with MUT-p53.

Genes	Gene names	Function
<i>C11orf41/ KIAA1549L</i>	KIAA1549-like; Chromosome 11 open reading frame 41	
<i>C3orf15/ MAATS1</i>	MYCBP-associated, testis expressed; Chromosome 3 open reading frame 15	May play a role in spermatogenesis.
<i>CALR FOXRED2</i>	Calreticulin FAD-dependent oxidoreductase domain-containing protein 2	Ca(2+)-binding chaperone. May function in endoplasmic reticulum associated degradation through binding and subsequent ubiquitination.
<i>FXR2</i>	Fragile X mental retardation, autosomal homolog 2	RNA-binding.

(2) Significantly downregulated genes in MDM2+ DLBCLs with WT-p53 or with MUT-p53.

Genes	Gene names	Function
<i>MRS2</i>	Magnesium homeostasis factor homolog (S. Cerevisiae)	Magnesium transporter into the mitochondrial matrix.
<i>PMS2L1</i>	Postmeiotic segregation increased 2 pseudogene1	
<i>PMS2L2</i>	Postmeiotic segregation increased 2 pseudogene2	
<i>PMS2L5</i>	Postmeiotic segregation increased 2 pseudogene5	
<i>TMEM216</i>	Transmembrane protein 216	Part of the tectonic-like complex.
<i>YWHAB</i>	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, Beta /14-3-3 protein beta/alpha	Adapter protein mediating signal transduction by binding to phosphoserine-containing proteins.

Supplemental Table 2. Common genes that are both significantly differentially expressed between patients with MDM2+ and MDM2– DLBCL with WT-p53 (*P* value cutoff: .0012, false discovery rate for multiple t-tests: .30), and between patients with p53+ and p53– DLBCL with WT-p53 (*P* value cutoff: .0035, false discovery rate: .30). The major gene function is according to the UniProt Knowledgebase (<http://www.uniprot.org>).

(1) Significantly upregulated genes in MDM2+ or p53+ DLBCLs with WT-p53.

Genes	Gene names	Function
<i>B3GAT2</i>	Beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S)	Transmembrane protein involved in the biosynthesis of L2/HNK-1 carbohydrate epitope on both glycolipids and glycoproteins.
CACYBP	Calcyclin-binding protein	Involved in calcium-dependent ubiquitination and subsequent proteasomal degradation of target proteins.
<i>CCL22</i>	C-C motif chemokine 22	Cys-Cys(CC) cytokines that may play a role in the trafficking of activated/effector T-lymphocytes to inflammatory sites and other aspects of activated T-lymphocyte physiology.
CDKN1A	Cyclin-dependent kinase inhibitor 1 (p21, Cip1)	Cell cycle arrest.
<i>FSCN1</i>	Fascin	Organizes filamentous actin into bundles; play a role in cell migration, motility, adhesion and cellular interactions.
<i>GDA</i>	Guanine deaminase	Catalyzes the hydrolytic deamination of guanine producing xanthine and ammonia.
<i>ITPKA</i>	Inositol-trisphosphate 3-kinase A	Second messenger inositol 1,4,5-trisphosphate 3-kinase and a substrate for the cyclic AMP-dependent protein kinase, calcium/calmodulin- dependent protein kinase II, and protein kinase C in vitro.
<i>KDELRL2</i>	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	Required for the retention of luminal endoplasmic reticulum protein.
<i>KREMEN1</i>	Kringle containing transmembrane protein 1	Receptor for Dickkopf protein. Cooperates with Dickkopf to block Wnt/beta-catenin signaling.
MDM2	Mdm2, p53 E3 ubiquitin protein ligase homolog (mouse)	E3 ubiquitin-protein ligase that mediates ubiquitination of p53, leading to its degradation by the proteasome.
MMP1	Matrix metalloproteinase 1 (interstitial collagenase)	Proteases involved in collagen degradation.

<i>PTPRR</i>	protein tyrosine phosphatase, receptor type, R	Sequesters mitogen-activated protein kinases (MAPKs) such as MAPK1, MAPK3 and MAPK14 in the cytoplasm in an inactive form.
<i>SEC24A</i>	SEC24 family, member A (S. Cerevisiae)	Component of coat protein II-coated ER-derived vesicles involved in protein transport from the endoplasmic reticulum to the Golgi apparatus.
<i>SEN3</i>	SUMO1/sentrin/SMT3 specific peptidase 3	Protease that releases SUMO2 and SUMO3 monomers from sumoylated substrates.
<i>SLC25A4</i>	Solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 4	Exchanges cytoplasmic ADP with mitochondrial ATP across the mitochondrial inner membrane.
<i>SLC43A2</i>	Solute carrier family 43, member 2	Sodium-, chloride-, and pH-independent high affinity transport of large neutral amino acids.
<i>UBE2NL</i>	Ubiquitin-conjugating enzyme E2N-like	A member of the ubiquitin-conjugating enzyme family.

Note: *CACYBP*, *CDKN1A*, *MDM2*, and *MMP1* are p53 target genes. *SEN3* attenuates MDM2-mediated p53 ubiquitination and degradation.

(2) Significantly downregulated genes in MDM2+ or p53+ DLBCLs with WT-p53.

Genes	Gene names	Function
<i>ARID5B</i>	AT rich interactive domain 5B (MRF1-like)	Forms a histone H3K9Me2 demethylase complex with PHD finger protein 2 involved in gene transcription activation.
<i>ATM</i>	Ataxia telangiectasia mutated	Serine/threonine protein kinase.
<i>CD47</i>	CD47 molecule	Leukocyte surface antigen, involved in calcium influx, membrane transport, signal transduction, cell adhesion.
<i>CD52</i>	CD52 molecule	CAMPATH-1 antigen that may play a role in carrying and orienting carbohydrate.
<i>CD53</i>	CD53 molecule	Leukocyte surface antigen, involved in signal transduction and growth regulation in hematopoietic cells.
<i>CD72</i>	CD72 molecule	B-cell differentiation antigen that plays a role in B-cell proliferation and differentiation.
<i>CP</i>	Ceruloplasmin	A copper-binding glycoprotein and involved in the peroxidation of Fe ²⁺ to Fe ³⁺ .
<i>FCRL1</i>	Fc receptor-like 1	An activating coreceptor in B-cells that

<i>FCRL2</i>	Fc receptor-like 2	may function in B-cells activation and differentiation. A member of the immunoglobulin receptor superfamily that may have an regulatory role in normal and neoplastic B-cells development.
<i>FCRL3</i>	Fc receptor-like 2	A member of the immunoglobulin receptor superfamily.
<i>FCRL5</i>	Fc receptor-like 2	A member of the immunoglobulin receptor superfamily that may be involved in B-cells development and differentiation.
<i>FKBP15</i>	FK506-binding protein 133kDa	May be involved in the cytoskeletal organization of neuronal growth cones.
<i>GGA2</i>	Golgi-associated, gamma adaptin ear containing, ARF binding protein 2	Plays a role in protein sorting and trafficking between the trans-Golgi network (TGN) and endosomes.
<i>HERC4</i>	HECT and RLD domain containing E3 ubiquitin protein ligase 4	Probable E3 ubiquitin-protein ligase involved in either protein trafficking or in the distribution of cellular structures.
<i>HLA-DRA</i>	Major histocompatibility complex, class II, DR alpha	Binds peptides derived from antigens that access the endocytic route of antigen presenting cells (APC) and presents them on the cell surface for recognition by the CD4 T-cells.
<i>JMJD1C</i>	Jumonji domain containing 1C	Probable histone demethylase that specifically demethylates 'Lys-9' of histone H3.
<i>LENG8</i>	Leukocyte receptor cluster (LRC) member 8	
<i>LOC100132726</i>		
<i>LOC730057</i>		
<i>MDM4</i>	Mdm4 p53 binding protein homolog (mouse)	Inhibits p53 by binding its transcriptional activation domain.
<i>PELI1</i>	Pellino E3 ubiquitin protein ligase 1	E3 ubiquitin ligase catalyzing the covalent attachment of ubiquitin moieties onto substrate proteins.
<i>RBM5</i>	RNA-binding motif protein 5	Regulates alternative splicing of a number of mRNAs including TP53.
<i>SMCHD1</i>	Structural maintenance of chromosomes flexible hinge domain-containing protein 1	Required for maintenance of X inactivation in females and hypermethylation of CpG islands associated with inactive X.
<i>TBC1D1</i>	TBC1 domain family member 1	May have a role in regulating cell growth and differentiation.
<i>TMCC1</i>	Transmembrane and coiled-coil domain family 1	
<i>U2AF1</i>	U2 small nuclear RNA auxiliary	Plays a critical role in both constitutive and

	factor 1	enhancer-dependent splicing by mediating protein-protein interactions and protein-RNA interactions required for accurate 3'-splice site selection.
<i>UBE2E1</i>	Ubiquitin-conjugating enzyme E2 E1	E2 ubiquitin-conjugating enzyme.
<i>USP39</i>	Ubiquitin specific peptidase 39	Plays a role in pre-mRNA splicing as a component of the U4/U6-U5 tri-snRNP, one of the building blocks of the spliceosome.
<i>WTAP</i>	Wilms tumor 1 associated protein	Regulates G2/M cell-cycle transition by binding to the 3' UTR of CCNA2, which enhances its stability.
<i>YLPM1</i>	YLP motif-containing 1	Plays a role in the reduction of telomerase activity during differentiation of embryonic stem cells by binding to the core promoter of TERT and controlling its down-regulation.
<i>ZCCHC6</i>	Zinc finger, CCHC domain containing 6	Uridyltransferase that mediates the terminal uridylation of some specific RNAs.
<i>ZCCHC7</i>	Zinc finger, CCHC domain containing 7	Nucleic acid binding.

Note: *ATM*, *MDM4*, and *RBM5* have interaction with the TP53 pathway.

Supplemental Table 3. Genes significantly differentially expressed between patients with MDM2+ and MDM2– DLBCL with MUT-p53 with > 2 fold change (*P* value cutoff: .0023, false discovery rate for multiple t-tests: .30). The major gene function is according to the UniProt Knowledgebase (<http://www.uniprot.org>).

(1) Genes significantly upregulated in MDM2+ patients with MUT-p53.

Genes	Gene names	Biological process	Function
<i>ZNF827</i>	Zinc finger protein 827	Transcription	Transcriptional regulation.
<i>CXCL5</i>	Chemokine (C-X-C motif) ligand 5	Signaling	Involved in neutrophil activation.
<i>FLCN</i>	Folliculin	Protein phosphorylation	May play a role in pathogenesis yet may be a tumor suppressor.
<i>MXD1</i>	MAX dimerization protein 1	Transcription	Transcriptional repressor protein antagonizing MYC-mediated transcriptional activation.
<i>SYMPK</i>	Symplekin	Cell adhesion; mRNA processing	Component of heat-sensitive complex functioning in histone mRNA 3'-end processing and component of cell junction.
<i>RBM8A</i>	RNA binding motif protein 8A	mRNA processing	Involved in mRNA metabolism.
<i>SLC25A37</i>	Solute carrier family 25, member 37	Transport	Mitochondrial iron transporter.
<i>DCAF8</i>	DDB1- and CUL4-associated factor 8	Protein ubiquitination	Maybe receptor for CUL4-DDB1 E3 ubiquitin-protein ligase complex.

Note: *CXCL5* gene activation might be the gain-of-function of p53 mutant.

(2) Genes significantly downregulated in MDM2+ patients with MUT-p53.

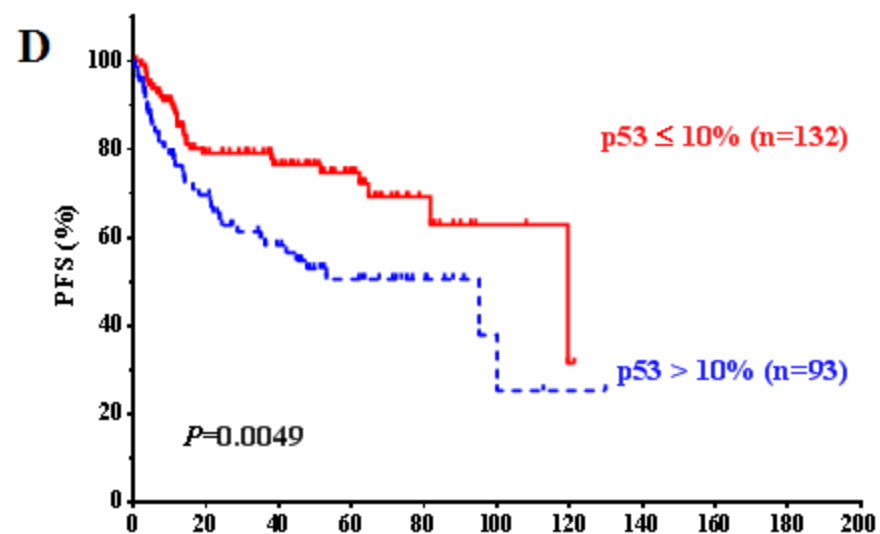
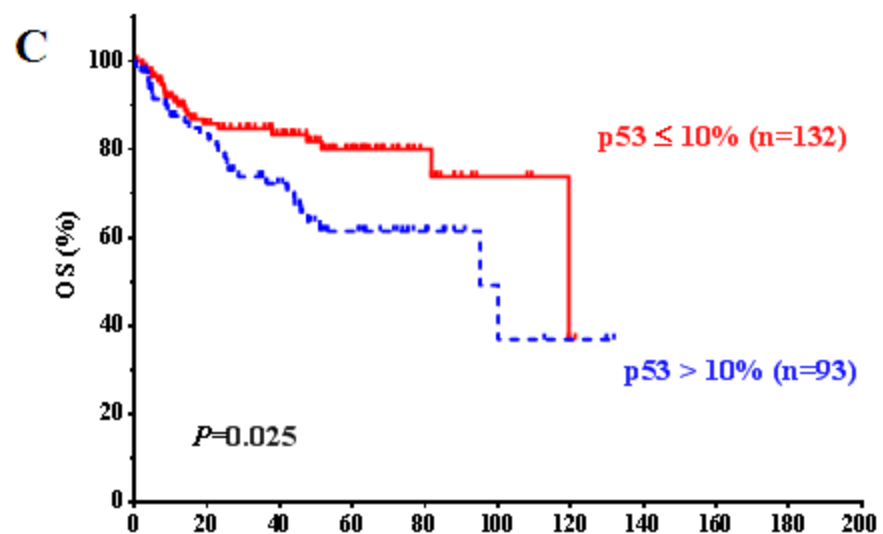
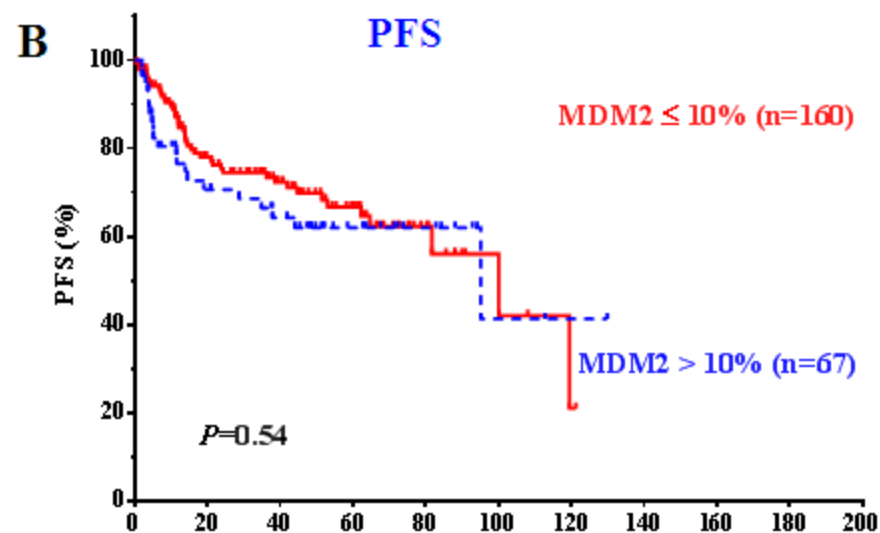
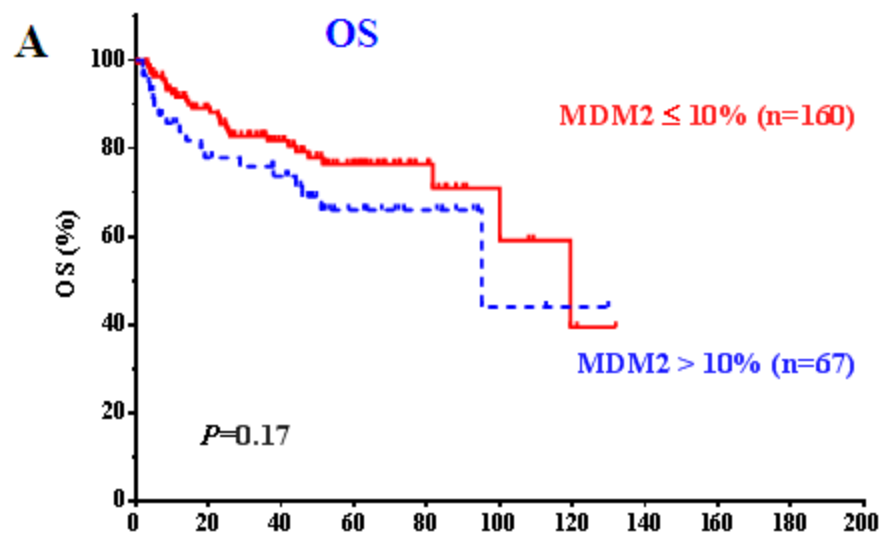
Genes	Gene names	Biological process	Function
<i>CDC42SE2</i>	CDC42 small effector 2	Structure	Interacting with CDC42, maybe involved in inducing actin filament assembly, F-actin accumulation, and phagocytosis.
<i>YIPF5</i>	Yip1 domain family, member 5	Transport	Transportation between endoplasmic reticulum and Golgi.
<i>EIF2A</i>	Eukaryotic translation initiation factor 2A, 65kDa	Metabolism	Protein synthesis.

<i>ATP5C1</i>	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, gamma polypeptide 1 protein 97	Metabolism	Mitochondrial ATP synthase.
MBD4	Methyl-CpG binding domain protein 4	DNA repair	DNA repair.
<i>UBQLN2</i>	Ubiquilin 2	Metabolism	Increases the half-life of proteins to be degraded by the proteasome.
PAK2	p21 protein (Cdc42/Rac)-activated kinase 2	Apoptosis	Full-length PAK2 stimulates cell survival and cell growth while cleaved PAK2 promotes cellular apoptosis; caspase-activated PAK2 reduces cellular translation.
<i>SPCS1</i>	Signal peptidase complex subunit 1 homolog (<i>S. cerevisiae</i>)	Metabolism	Removes signal peptides from nascent proteins in the endoplasmic reticulum.
<i>HIST1H1C</i>	Histone cluster 1, H1c	Structure	The linker histone H1 condenses nucleosome chains.
<i>INTS6</i>	Integrator complex subunit 6	Metabolism	Component of the Integrator complex which is involved in the snRNA U1 and U2 transcription and in their 3'-box-dependent processing.
<i>ATAD2</i>	ATPase family, AAA domain containing 2	Transcription	May be a transcriptional coactivator (inducing estradiol target genes, such as CCND1, MYC and E2F1); May be required for histone hyperacetylation.
<i>KIN</i>	Antigenic determinant of recA protein homolog (mouse)	DNA repair	Involved in DNA replication and repair.
<i>MBNL1</i>	Muscleblind-like splicing regulator 1	mRNA processing	Mediates pre-mRNA alternative splicing regulation.
<i>SCP2</i>	Sterol carrier protein 2	Metabolism	Transfer non-specific lipid between membranes.
<i>ATP5E</i>	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, epsilon subunit	Metabolism	Mitochondrial ATP synthase.
<i>C1orf156</i>	Methyltransferase like 18		Probable histidine methyltransferase (By similarity).
ATG7	ATG7 autophagy related 7 homolog (<i>S. cerevisiae</i>)	Autophagy	Conjugation of autophagy proteins.

<i>C10orf78</i>	SWI5-dependent recombination repair 1	DNA repair	DNA repair.
<i>DCUN1D1</i>	DCN1, defective in cullin neddylation 1, domain containing 1 (<i>S. cerevisiae</i>)	Signaling	Component of an E3 ubiquitin ligase complex for neddylation.
<i>DHX40</i>	DEAH (Asp-Glu-Ala-His) box polypeptide 40		Probable ATP-dependent RNA helicase (By similarity).
<i>STYX</i>	Serine/threonine/tyrosine interacting protein		Probable pseudophosphatase.

Note: *MBD4*, *PAK2*, *ATG7*, and *DCUN1D1* have interaction with the TP53 pathway.

Supplemental Figure 1. Impact of MDM2 and p53 expression on overall and progression-free survival in a DLBCL validation set. **(A-B)** MDM2 overexpression did not correlate with poor survival in DLBCL. **(C-D)** p53 overexpression correlated with significant poor survival in DLBCL.



Months

Months