Research Focus

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p53: Choice of Response – Repair or Death

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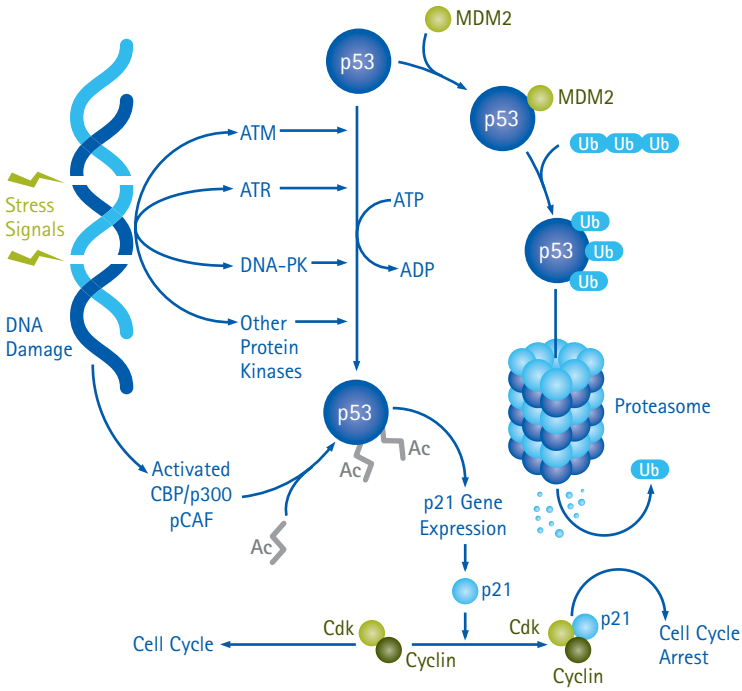
The p53 family of transcription factors includes p53, p63, and p73, each of which has an important role in DNA damage response. p53, a well-conserved phosphoprotein, is one of the best known tumor suppressors.

Human p53 consists of 393 amino acids assembled into five structurally and functionally different domains: an acidic N-terminal region, which contains the 42 amino acid transactivation domain, followed by a hydrophobic, proline-rich region (amino acids 64 to 92), a central sequence-specific DNA-binding domain (amino acids 102 - 292), a tetramerization domain (amino acids 324 - 355), and a highly basic C-terminal region regulatory domain (amino acids 363 - 393). p53 is a sequence-specific nuclear transcription factor that binds to defined consensus sites within DNA as a tetramer and represses transcription of a set of genes involved in cell growth stimulation, while activating a different set of genes involved in cell cycle control. It causes growth arrest before either DNA replication in the G_1 phase or mitosis in the G_2 phase. This provides a window for DNA repair or elimination of cells with severely damaged DNA strands.



Transcription-independent apoptosis activation by p53

In some cell types, however, p53 activation results in apoptosis as a means of eliminating severely damaged cells. In addition to p53's activation of transcription of proapoptotic genes, p53 can also trigger apoptosis through transcription-independent mechanisms. *In vitro* studies have shown that p53 can bind to Bcl2 family proteins, such as Bax, Bak and Bcl-XL, in the mitrochondrial membrane, activating cytochrome c release and caspase cascades. *In vivo* studies have shown that γ-irradiated mice display translocation of p53 to mitochondria in advance of p53-activated transcription. More *in vivo* studies are in progress to define the physiological relevance of the molecular mechanisms by which p53 exerts its transcription-independent effects.

Activation of p53 during carcinogenesis

In normal, non-activated cells, the p53 signaling network is not active. However, p53 signaling is activated in cells as a response to various signals that take place during the carcinogenic process. Carcinogen-induced DNA damage, abnormal proliferative signals, hypoxia, and loss of cell adhesion are some of the most common signals that activate p53. The final outcome of p53 activation depends on many factors, and is mediated largely through the action of downstream effector genes transactivated by p53. Agents that damage DNA induce p53 to become very stable by post-translational mechanisms, allowing its concentration in the nucleus to increase dramatically. Hence, p53 is likely to suppress tumors by ensuring genomic integrity and repressing proliferation of tumor-forming cells.

MDM2: The regulator of p53 degradation

In unstressed cells, p53 is latent and is maintained at low levels by targeted, ubiquitin-mediated degradation mediated by MDM2 and many other ubiquitin ligases. MDM2, a p53-inducible phosphoprotein, binds to the N-terminus of the p53 and negatively regulates its activity. Transcription of MDM2 is activated by p53. Hence, in the presence of high levels of p53, MDM2 levels are also elevated. p53 interacts with MDM2 at Phe^{19}, Trp^{23}, and Leu^{26} to fill up a complementary hydrophobic pocket of MDM2. The three amino acids are also essential for transactivation of p53. Binding of MDM2 to p53 antagonizes the transcriptional activity of p53 and blocks its acetylation and transactivation by interfering with p300/CBP.

MDM2 functions as an E3 ligase to ubiquitinate p53 and force its export from the nucleus to the cytoplasm, where p53 is degraded by the proteasome. The E3 ubiquitin ligase activity of MDM2 alone, however, is not sufficient to trigger p53 degradation. MDM2 mono-ubiquitinates p53 at multiple sites but does not catalyze the addition of polyubiquitin chains, which are essential for recognition by the proteasome. Monoubiquitination of p53 may expose a nuclear export signal; polyubiquitination and degradation can then proceed in the cytoplasm. Although p53-mediated transactivation is a nuclear event, p53 degradation occurs in the cytoplasm. Hence, the ubiquitin ligase function of MDM2 might serve as a cellular mechanism for turnover of p53-MDM2 complexes after their function is completed.

The nuclear export signal of MDM2 is required for p53 degradation. Studies have shown that Leptomycin B, a blocker of nuclear export complex formation, also prevents nuclear-cytoplasmic shuttling of MDM2 and p53. p53, if sequestered in the cytoplasm, is resistant to degradation by MDM2. Import of p53 from cytoplasm to nucleus and export back to cytoplasm seems to be essential for its degradation, and the shuttling of MDM2 and p53 may be a mechanism to prevent their premature degradation.

Overexpression of MDM2 in tumors

When normal mammalian cells are subjected to stress signals, such as hypoxia, radiation, and chemotherapeutic drugs, p53 is phosphorylated at multiple sites, including those involved in its binding to MDM2. This leads to its activation and blockage of its ubiquitin-dependent degradation. On the other hand, in a number of human tumors, p53 is inactivated by overexpression of MDM2. Malignant tumors, particularly breast tumors and soft tissue sarcomas, are reported to frequently overexpress MDM2. In breast cancer cells, overexpression of MDM2 is correlated with lack of p21 expression. However, over-expression of MDM2 in normal cells is known to cause G_1 arrest. Hence, MDM2 induced by DNA damage in normal cells may have a protective role in preventing untimely cell cycle progression.

Phosphorylation of p53

Human p53 is phosphorylated at least at 23 different sites by stress-activated protein kinases, DNA Protein kinase (DNA-PK), casein kinase I and II, and cyclin-dependent kinases. Although the exact functions of specific phosphorylation at various sites is still controversial, evidence indicates that phosphorylation of p53 provides stability by promoting its dissociation from MDM2 and enhancing its transcriptional activity. Most of the p53 phosphorylation sites are clustered within the 40 amino acids at its N-terminal region. ATM and ATR kinases promote phosphorylation of human p53 at Ser^{15} and Ser^{20}, which are essential for the activation of p53 following DNA damage. DNA-PK phosphorylates Ser^{15} within the critical N-terminal region of p53, which controls the interaction of p53 with the transcriptional apparatus and with the MDM2 protein. DNA-PK also phosphorylates Ser^{9} and Thr^{18}; however, phosphorylation at these sites is dependent upon the presence of the full-length p53, and is independent of phosphorylation at other sites. Phosphorylation at Thr^{18} alters the structure of the amphipathic α-helix with which MDM2 interacts. Studies have shown that when p53 co-localizes with DNA-PK and ssDNA, there is a 10-fold enhancement of p53 phosphorylation. Casein Kinase I can also phosphorylate Ser^{9} and Thr^{18}, however, these phosphorylations are dependent upon prior phosphorylation of Ser^{6} and Ser^{15}. All types of tumor cells exhibit higher levels of p53 phosphorylation when compared to normal non-transformed cells. These phosphorylations offer greater stability to p53 regardless of p53 mutations.

Acetylation of p53

In spite of extensive studies on p53 phosphorylation, it is now known that phosphorylation is not the only mechanism that regulates activation of p53. Following cellular stress, p53 is shown to be acetylated by CBP/p300 at multiple lysine residues ($Lys^{370, 372, 373, 381, and 382}$) and by pCAF at Lys^{320}. The precise *in vivo* roles of these acetylation sites remains to be completely elucidated; transgenic mice bearing mutations at these lysine residues have shown differing, cell type-specific phenotypes, indicating that control of p53 by acetylation may require combinatorial effects of multiple acetylation sites. *In vitro* studies show that increasing the level of p53 acetylation with deacetylase inhibitors prevents p53 from degradation. HDAC1 and SIRT1 are among the deacetylases that may be responsible for regulating p53. Overexpression of MDM2 is also shown to effectively reduce p300-dependent p53 acetylation, further supporting the importance of acetylation.

Mutations in p53

p53 is shown to be either non-functional or mutated in most human cancers. The most common anomaly of p53 in human cancers is mutation of the p53 gene. A large number of mutations are caused by single base substitutions, and about 30% of these mutations are reported to occur in hotspot codons. Functional p53 provides a protective mechanism against tumor growth, and a loss of p53 function is a key step in the neoplastic cascade. In addition, the function of p53 is critical to the success of many cancer treatments since radiation and chemotherapy act in part by triggering cell suicide in response to DNA damage. A successful response to therapy is greatly reduced in tumors where mutant p53 is present, and these tumors are often very difficult to treat. Therefore, genome-wide association studies and individual genetic analyses of p53 mutations in individuals and tumors may be a powerful means for patient stratification in clinical trials and an effective approach for "precision medicine."

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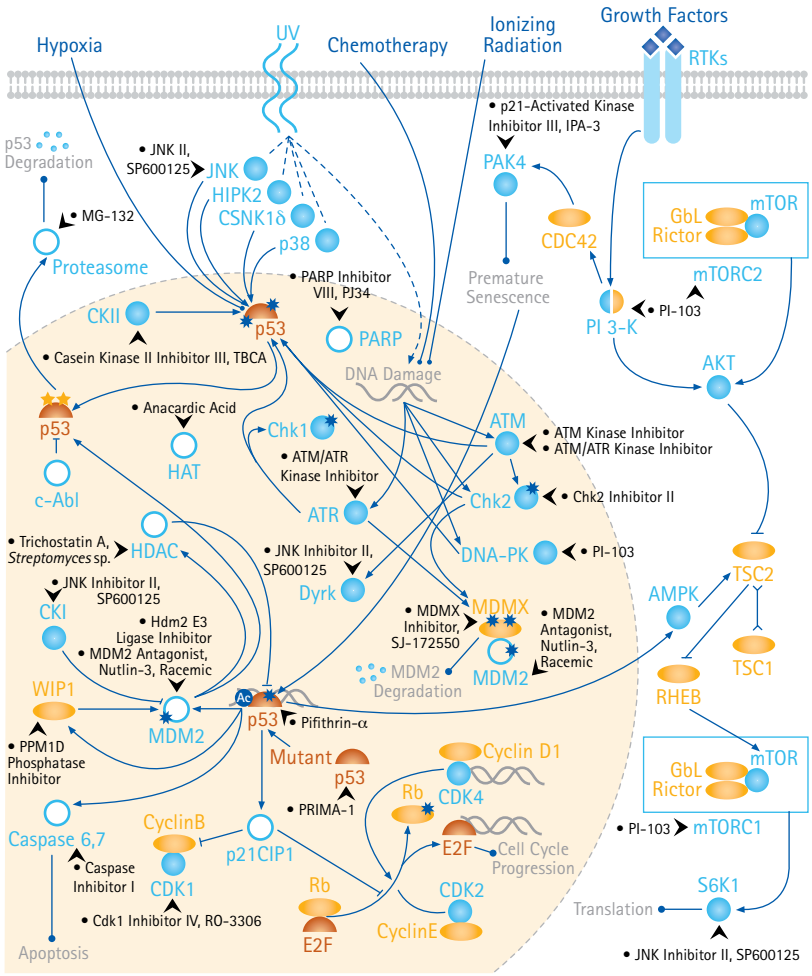
InhibitorSelect™ p53 Pathway Regulators Panel

(Catalogue No. 506169)

The InhibitorSelect™ p53 Pathway Regulators Panel (Catalogue No. 506169) enables multiparameter analysis, assessment of signal amplification/feedback and comparison of biological effects of perturbing different parts of the pathway.



Phosphorylation

Ubiquitin

Calbiochem® Inhibitors

The Inhibitor panel includes:

Description	Qty/Pk	Catalogue No.
ATM Kinase Inhibitor	2 mg	118500
ATM/ATR Kinase Inhibitor	5 mg	118501
Anacardic Acid	10 mg	172050
Cdk1 Inhibitor IV, RO-3306	5 mg	217699
Casein Kinase II Inhibitor III, TBCA	5 mg	218710
Chk2 Inhibitor II	1 mg	220486
Hdm2 E3 Ligase Inhibitor	5 mg	373225
JNK Inhibitor II	5 mg	420119
MDM2 Antagonist, Nutlin-3, Racemic	5 mg	444143
MDMX Inhibitor, SJ-172550	10 mg	444155
MG-132	5 mg	474790
p21-Activated Kinase Inhibitor III, IPA-3	5 mg	506106
Pifithrin-α	1 mg	506132
PI-103	5 mg	528100
PARP Inhibitor VIII, PJ34	1 mg	528150
PPM1D Phosphatase Inhibitor	10 mg	529578
PRIMA-1	10 mg	530050
Caspase Inhibitor I	1 mg	627610
Trichostatin A, Streptomyces sp.	1 mg	647925
Anhydrous DMSO	15 mL	KP31817

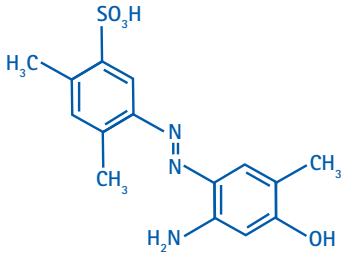
FEATURED p53 PATHWAY ACTIVATORS

Description	Comments	Qty/Pk	Catalogue No.
p53 Activator, Cell-Permeable	A synthetic cell-permeable peptide corresponding to the C-terminal amino acids 361 - 382 of p53. Binds mutant p53 and restores the growth suppressor functions of p53 protein in human tumor cells.	500 µg	506131
p53 Activator II, Cell-Permeable	A cell-permeable, proteolytically stable p53-activating peptide that displays antitumor properties.	500 µg	506144
p53 Activator III, RITA	A cell-permeable, p53-targeting, tricyclic thiophene derivative that blocks p53-MDM2 interaction and p53 ubiquitination and induces p53-dependent apoptosis in tumor cells expressing wild-type p53.	1 mg	506149
PRIMA-1	A cell-permeable quinuclidinone analog that restores biochemical and biological function to mutant p53 and induces p53-dependent apoptosis *in vitro* and *in vivo*.	10 mg	530050
p53 Activator VII, STIMA-1	A cell-permeable compound that covalently modifies free thiols on mutant p53 in H1299-His^{175} cells and fully restore its DNA binding activity to the level seen with wild-type p53, resulting in upregulation of p53-dependent gene expression.	25 mg	506168
p53 Modulator, CP-31398	A cell-permeable compound that protects wild-type p53 against heat-induced denaturation and locks newly synthesized mutant p53 in an active conformation. Unlike PRIMA-1, it directly targets the DNA binding domain of p53.	5 mg	506166
p53-Snail binding Inhibitor, GN25	A cell-permeable, specific p53-Snail binding inhibitor that activates p53 in a K-Ras-dependent manner and displays anti-proliferating effect toward K-Ras-transformed mouse embryonic fibroblasts. Selectively activates wild-type p53 in p53WT/MT cancer cells.	25 mg	506170
Mutant p53 Reactivator, RETRA	A cell-permeable compound that upregulates p53 family-responsive element-dependent reporter plasmid transcription activity in cells bearing Glu^{266}, His^{273}, Lys^{280}, or Trp^{278} mutant p53 by increasing the cellular protein, but not mRNA, level of the p53 homologue p73 and by disrupting p73 interaction with mutant p53.	5 mg	506164
Tenovin-1	A cell-permeable compound that up-regulates cellular p53 protein, but not mRNA, level in MCF-7 (≥6-fold in 6 h), presumably by blocking MDM2-mediated p53 degradation.	10 mg	580566

Ischemin

(Qty: 25 mg, Catalogue No. 410960)

A cell-permeable compound that blocks CBP-p53 interaction and alters the post-translational modification states on p53 and histones. Inhibits transcription functions of p53 on DNA damage (IC_{50} = 5 µM for p53-induced p21 activation in Luc-U2OS cells) and is shown to suppress cardiac myocyte apoptosis during ischemic conditions. **Purity**: ≥99% by HPLC. M.W. 335.4.



Pifithrin-µ

(Phenylacetylenylsulfonamide)

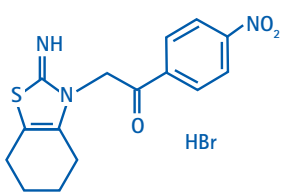
(Qty: 10 mg, Catalogue No. 506155)

A cell-permeable blocker of p53 interaction with Bcl-xL and Bcl-2 proteins. Selectively inhibits p53 translocation to mitochondria without affecting the transactivation function of p53. Targets only the mitochondrial p53 pathway without affecting the important transcriptional functions of p53. **Purity**: ≥95% by HPLC. M.W. 181.2.

Pifithrin-α, *p*-Nitro

(Qty: 5 mg, Catalogue No. 506152)

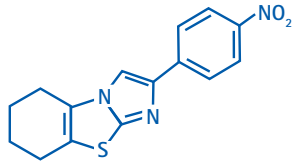
A cell-permeable p53 inhibitor that serves as the prodrug form of Pifithrin-α, *p*-Nitro, Cyclic (Catalogue No. 506154). **Purity**: ≥97% by HPLC. M.W. 398.3.



Pifithrin-α, *p*-Nitro, Cyclic

(Qty: 5 mg, Catalogue No. 506154)

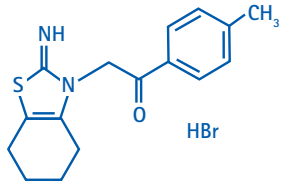
A cell-permeable p53 inhibitor with 10-fold higher potency (ED_{50} = 30 nM in protecting etoposide-induced cortical neuron death) and 50% longer half-life than Pifithrin-α (Catalogue No. 506132). **Purity**: ≥97% by HPLC. M.W. 299.4.



Pifithrin-α

(Qty: 5 mg/10 mg, Catalogue No. 506132)

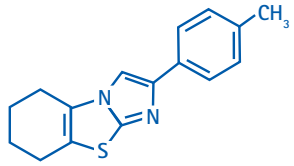
A cell-permeable chemical inhibitor of p53. Reversibly inhibits p53-dependent transactivation of p53-responsive genes and reversibly blocks p53-mediated apoptosis. **Purity**: ≥95% by HPLC. M.W. 367.3.



Pifithrin-α, Cyclic-

(Qty: 10 mg, Catalogue No. 506134)

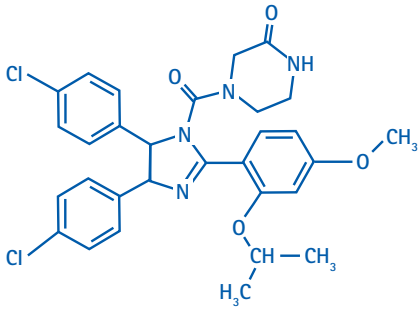
A cell-permeable, very stable analog of Pifithrin-α (Catalogue No. 506132), with similar biological function, but with reduced cytotoxicity. **Purity**:≥ 95% by HPLC. M.W. 349.3.



MDM2 Antagonist, Nutlin-3, Racemic

(Qty: 1 mg, Catalogue No. 444143)

A cell-permeable cis-imidazoline compound that acts as a potent and selective MDM2 antagonist (IC_{50} = 90 nM for Nutlin-3a and 13.6 µM for Nutlin-3b). Activates p53 pathway by binding MDM2 in the p53-binding pocket and inhibits MDM2-p53 interaction. **Purity**: ≥98% by HPLC. M.W. 581.5



MDM2 Antagonist IV, Nutlin-3a

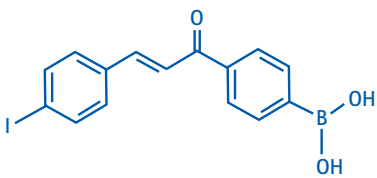
(Qty: 5 mg, Catalogue No. 444152)

A cell-permeable and highly potent active enantiomer of Nutlin-3 (Catalogue No. 444143) that binds to the p53-binding pocket and blocks the interaction of p53 and MDM2 (IC_{50} = 90 nM). **Purity**: ≥98% by HPLC. M.W. 581.5.

MDM2 Inhibitor (trans-4-Iodo, 4′-boranyl-chalcone)

(Qty: 10 mg, Catalogue No. 444145)

A cell-permeable boranyl-chalcone that binds strongly to MDM2 and irreversibly disrupts MDM2/p53 protein complex. Exhibits selective toxicity towards MDM2 overexpressing human breast cancer cell lines (IC_{50} = 10, 8.8, and 7 µM for MDA-MB-435, MDA-MB-231, and Wt-MCF-7, respectively) compared to normal breast cell lines (IC_{50} = 75 and 63 µM for MCF-10A and MCF-12A, respectively). **Purity**: ≥95% by HPLC. M.W. 378.0



MDM2 Antagonist II, NSC 66811 (7-(Anilino(phenyl)-methyl)-2-methyl-8-quinolinol)

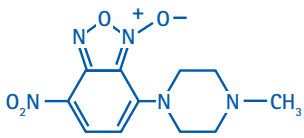
(Qty: 10 mg, Catalogue No. 444144)

A cell-permeable, non-peptidyl, quinolinol compound that binds MDM2 with high affinity (Ki = 120 nM) and disrupts MDM2-p53 interaction. Shown to dose-dependently induce cellular accumulation of p53, MDM2, and p21 in HCT-116 human colon cancer cell line with wild-type p53. **Purity**: ≥95% by HPLC. M.W. 340.4.

MDMX Inhibitor, NSC207895

(Qty: 10 mg, Catalogue No. 444158)

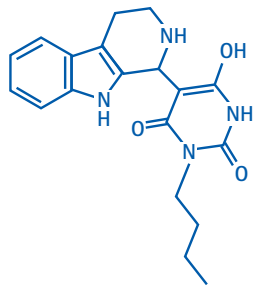
A cell-permeable compound that downregulates the p53 negative regulator MDMX protein level in MCF-7, LNCaP, and A549 cells (1 to 10 µM for 16 to 24 h) by suppressesing MDMX promoter transcription activity (IC_{50} = 2.5 µM in HT1080 reporter assays). **Purity**: ≥98% by HPLC. M.W. 279.3.



MDM2 Inhibitor VII, MEL23

(Qty: 10 mg, Catalogue No. 373227)

A cell-permeable compound that selectively inhibits the E3 ligase activity of MDM2-MDMX hetero-complex over that of MDM2-MDM2 homo-complex (70.6% vs. 17.6% inhibition, respectively, with 100 µM inhibitor), without affecting MDM2-MDMX complex. **Purity**: ≥95% by HPLC. M.W. 354.4.



ANTIBODIES FOR p53 RESEARCH

Description	Species	Applications	Catalogue No.
Anti-p53 (Ab-1) (Pantropic) Mouse mAb (PAb421)	Human, monkey, mouse, rabbit, rat	FC, FS, GS, IB, IF, IP	OP03
Anti-p53 (Ab-1) (Pantropic) Mouse mAb (PAb421)	Human, monkey, mouse, rabbit, rat	FC, FS, GS, IB, IF, IP	OP03L
Anti-p53 (Ab-1) (Pantropic) Mouse mAb (PAb421)	Human, monkey, mouse, rabbit, rat	FC, FS, IF	OP03F
Anti-p53 (Ab-2) (Pantropic) Mouse mAb (PAb1801)	Human	FS, GS, IB, IP, PS	OP09
Anti-p53 (Ab-6) (Pantropic) Mouse mAb (DO-1)	Feline, human	FS, GS, IB, IC, IP, PS	OP43
Anti-p53 (Ab-6) (Pantropic) Mouse mAb (DO-1)	Feline, human	FS, GS, IB, IC, IP, PS	OP43L
Anti-p53 (Ab-6) (Pantropic) Mouse mAb (DO-1) Agarose Conjugate	Feline, human	FS, GS, IB, IC, IP, PS	OP43A
Anti-p53 (Ab-6) (Pantropic) Mouse mAb (DO-1) Fluorescein Conjugate	Feline, human	FC, FS, IC, IF, PS	OP43F
Anti-p53 (Ab-7) (Pantropic) Sheep pAb	Human, mouse, rat	FS, IB, IF, IP, PS	PC35
Anti-p53 (Ab-11) (Pantropic) Mouse mAb (PAb1802)	Human, mouse	IB, IP	OP104L
Anti-p53 (Ab-12) (Pantropic) Mouse mAb (DO-7)	Bovine, human, monkey	FS, IB, IF, IP, PS	OP140
Anti-p53 (pantropic), clone DO-1	Human	IB, ICC, IHC, IF, IP	MABE327
Anti-p53 R2	Human, mouse, rat	IB	AB4052
Anti-p53, Clone Pab421	Mouse	IB, IP, IH	MABE283
Anti-p53 Antibody, clone E26	Human, rat	IB, IC, IH	04-241
Anti-p53 Antibody, clone E26	Human, rat	IB, IC, IH	Ab9985
Anti-p53 Antibody, aa 211-220, clone240	Bovine, chicken, human, hamster, mouse, monkey, rat	IB, IH, IP	CBL404
Anti-p53 Antibody, clone BP53-12	Human	IB, IH, IP	05-224
Anti-p53 (Ab-3) (Mutant) Mouse mAb (PAb240)	Bovine, chicken, hamster, human, mouse, rat	FC, FS, GS, IB, IF, IP, PS	OP29
Anti-p53 (Ab-3) (Mutant) Mouse mAb (PAb240)	Bovine, chicken, hamster, human, mouse, rat	FC, FS, GS, IB, IF, IP, PS	OP29L
Anti-p53 (Ab-4) (Wild type) Mouse mAb (PAb246)	Mouse, rat	IC, IP, PS	OP32
Anti-p53 (Ab-4) (Wild type) Mouse mAb (PAb246)	Mouse, rat	IC, IP, PS	OP32L
Anti-p53 (Wild type), Clone Pab1620	Human, mouse	IB, IH	MABE339
Anti-p53 (Ab-5) (Wild type) Mouse mAb (PAb1620)	Bovine, human, mouse, primate, rat.	FS, IF, IP, PS	OP33
Anti-acetyl-p53 (Lys^{320}) Antibody	Bovine, chimpanzee, human	IB	06-1283
Anti-acetyl-p53 (Lys^{373}) Antibody, clone EP356(2)AY	Human	IB, IC, IH(P)	04-1137
Anti-acetyl-p53 (Lys^{382}) Antibody, clone EPR358(2), Rabbit	Human	IB, IC	04-1146
Anti-acetyl-p53 Antibody (Lys^{373}, Lys^{382})	Most vertebrates	IB	06-758
Anti-acetyl-p53 (Lys^{373}) Antibody	Human	IB, IP	06-916
PhosphoDetect™ Anti-p53 (pSer15) (Ab-3) Rabbit pAb	Human, mouse, rat	FFS, IB, IC, IP, PS	PC386
PhosphoDetect™ Anti-p53 (pSer15) (Ab-6) Rabbit pAb	Human	IB, PS	PC461
PhosphoDetect™ Anti-p53 (pSer20) Rabbit pAb	Human. mouse	IB, IC, IF, PS	DR1023
PhosphoDetect™ Anti-p53 (pSer392) (Ab-4) Rabbit pAb	Human, mouse	IB	PC387
PhosphoDetect™ Anti-p53 (pSer392) Mouse mAb (9F4)	Human, mouse	ELISA, IB	506133
PhosphoDetect™ Anti-p53 (pSer46) Rabbit pAb	Human	IB, IC, IP	DR1024
Anti-phospho-p53 (Ser33) Antibody, clone EP2393Y	Human	IB, IC	MABE199
Anti-phospho-p53 (Ser6) Antibody, clone Y179	Human	IB, IC, IH, IP	04-540
Anti-phospho-p53 (Ser392) Antibody, clone EP155Y	Human, rat	IB, IC, IH(P), IC, IP	04-244
Anti-p53 (C-terminus) Antibody, clone E47	Human	FC, IB, ICC, IP	04-242
Anti-p53 (N-term) Antibody, clone Y5	Human, rat	IB, IC, IH(P), IP	04-1083
Anti-p53 Binding Protein 1 (Ab-1) Rabbit pAb	Human, mouse	IB, IF, IP	PC712
Anti-p53 Binding Protein 1 Mouse mAb (BP13)	Human	IB, IC, IP	DR1003
Anti-TP53BP2 Mouse mAb (3F8)	Human	ELISA, IB, IH (P)	AP1163

*ELISA: enzyme linked immunosorbent assay; FC: flow cytometry; FFS: free floating sections; FS: frozen sections; GS: gel shift; IB: immunoblotting, IC: immunocytochemistry; IF: immunofluorescence; IH: immunohistochemistry IP: immunoprecipitation; PS: paraffin sections

FEATURED KIT FOR p53 RESEARCH

p53 Antibody Sampler Kit

(Qty: 1 kit, Catalogue No. ASK07)

Contains 20 µg of each of the following antibodies:

Description	Catalogue No.
Anti-p53 (Ab-1) (Pantropic) Mouse mAb (PAb421)	OP03
Anti-p53 (Ab-2) (Pantropic) Mouse mAb (PAb1801)	OP09
Anti-p53 (Ab-3) (Mutant) Mouse mAb (PAb240)	OP29
Anti-p53 (Ab-4) (Wild type) Mouse mAb (PAb246)	OP32
Anti-p53 (Ab-5) (Wild type) Mouse mAb (PAb1620)	OP33
Anti-p53 (Ab-6) (Pantropic) Mouse mAb (DO-1)	OP43

ANTIBODIES FOR MDM2 RESEARCH

Description	Species	Applications	Catalogue No.
Anti-MDM2 (Ab-1) Mouse mAb (IF2)	Human	FS, IB, IF, IP, PS	OP46
Anti-MDM2 (Ab-2) Mouse mAb (2A10)	Human	IB, IF, IP, PS	OP115
Anti-MDM2 (Ab-4) Mouse mAb (2A9C1.18)	Human, mouse	IB, IF, IH (P), IP	OP144
Anti-MDM2 (Ab-3) Mouse (4B11) Antibody	Human , mouse	IB, IF, IH (P), IP	OP143
Anti-MDM2 (Ab-5) Mouse mAb (4B2C1.11)	Human	IB, IF, IH (P), IP	OP145
Anti-MDM2 (Ab-6) Mouse mAb (5B10C)	Human	IB, IF, IH(P), IP	OP146
PhosphoDetect™ Anti-MDM2 (pSer166) Rabbit pAb	Human, mouse, rat	IB	DR1027
Anti-MDMx Antibody, clone 8C6	Human	IB, IP, IC, IH, FC	04-1555
Anti-MDM2 Antibody, clone 3G9	Human, mouse	IB, IP, IC, IH	04-1530
Anti-MDM4 Antibody, clone 7A8	Human, mouse	IB	04-1556
Anti-MDM2, Clone IF2	Human	IB, IH	MABE340
Anti-MDM2, Clone 2A10	Human	IB, IP	MABE281
Anti-MDM2, Clone 4B2C1.11	Human. mouse	IB, IC, IP	MABE331

FEATURED KIT FOR MDM2 RESEARCH

MDM2 Antibody Sampler Kit–Human

(Qty: 1 kit, Catalogue No. ASK26)

Each antibody is suitable for immunoblotting, immunoprecipitation, immunofluorescence, and immunohistochemistry (paraffin sections).

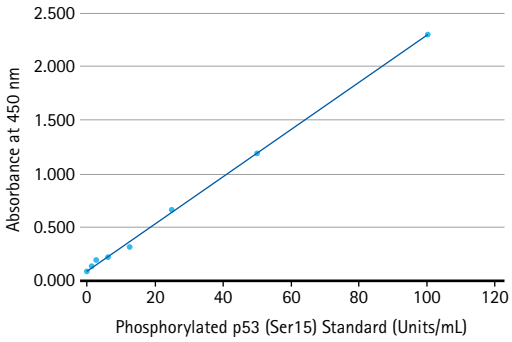
Contains 20 µg of each of the following antibodies:

Description	Catalogue No.
MDM2 (Ab-4) Monoclonal (2A9C1.18)	OP144
MDM2 (Ab-5) Monoclonal (4B2C1.11)	OP145
MDM2 (Ab-6) Monoclonal (5B10C1)	OP146

Phospho-p53 (Ser15) STAR ELISA Kit

(Qty: 1 kit (96 assays), Catalogue No. 17-475)

The colorimetric STAR (Signal Transduction Assay Reaction) ELISA kit is a solid phase sandwich enzyme linked immunosorbent assay that provides a fast, sensitive method to detect specific levels of signaling targets in whole cell extracts. The p53 plate is coated with a specific mouse monoclonal p53 capture antibody on the microwells of the 96-well clear plate. Sample lysate or standard included in the kit are incubated in the microwells allowing p53 antigen to be captured in the plate wells. The plate is then washed and wells are incubated with a specific rabbit anti-phospho-p53 (Ser15) antibody to detect the captured p53 phosphorylated on Ser15. After the addition of TMB substrate and stop solution the absorbance is measured at 450 nm.



p53 ELISA^{PLUS} (Autoantibody) Kit

(Qty: 1 kit, Catalogue No. QIA53)

Designed to measure circulating antibodies to p53 in human serum samples. Provided in a 96-well format. Plate is pre-coated with recombinant human wild-type p53. The detector antibody used is purified goat anti-human polyclonal antibody conjugated with horseradish peroxidase. Assay range: 0.16 - 1 antibody titer units

p53

(Qty: 10 µg, Catalogue No. 23-034)

N-terminal c-Myc, 6His-tagged, recombinant human p53 full length, expressed by baculovirus in Sf21 insect cells. Purified using immobilized metal affinity chromatography. **Purity**: ≥82% by SDS-PAGE. M.W. = 49,000.

Ref.: Matlashewski G. et al., 1984. EMBO J. 3, 3257.

p53, Wild-Type, His•Tag®, Human, Recombinant, *S. frugiperda*

(Qty: 5000 units, Catalogue No. 506147)

Human p53 expressed in a baculovirus expression system. Activity: 1 unit/ng protein. Biological activity: **Purity**: ≥95% by SDS-PAGE. M.W. 53,000.

Ref.: Liu, G., et al. 2003. J. Biol. Chem. 278, 17557; Zhang, L., et al. 2000. Cancer Res. 60, 3655; Bennett, W.P., et al. 1992. Chest 101, 19S; Hollstein, M., et al. 1991. Science 253, 49; Fields, S., and Jang, S.K. 1990.

p53, His•Tag®, Human, Recombinant, *E. coli*

(Qty: 10 µg, Catalogue No. 506165)

Recombinant, human, wild-type p53 fused at the N-terminus to a His•Tag® sequence and expressed in E. coli. p53, a tumor suppressor, blocks transformation and inhibits tumor cell growth. The purified protein is useful in DNA binding assays and as a protein kinase substrate. **Purity**: ≥80% by SDS-PAGE.

p53 Activating Ligand

(Qty: 500 µg, Catalogue No. 25-006)

Peptide corresponding to the cell membrane-translocating sequence (MTS, Catalogue Bo. 25-003) linked to the single-stranded DNA binding region of human p53, 'peptide 46', corresponding to amino acids 361-382 (AAVALLPAVLLALLAPGSRAHSSHLKSKKGQSTSRHKK). M.W. = 3932. **Purity**: ≥98% as determined by HPLC. Peptide content 72.3%.

Ref.: Selivanova, G., et al., 1997. Nat. Med. 3, 632; Selivanova, G., et al., 1996. Nucleic Acids Res. 24, 3560

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