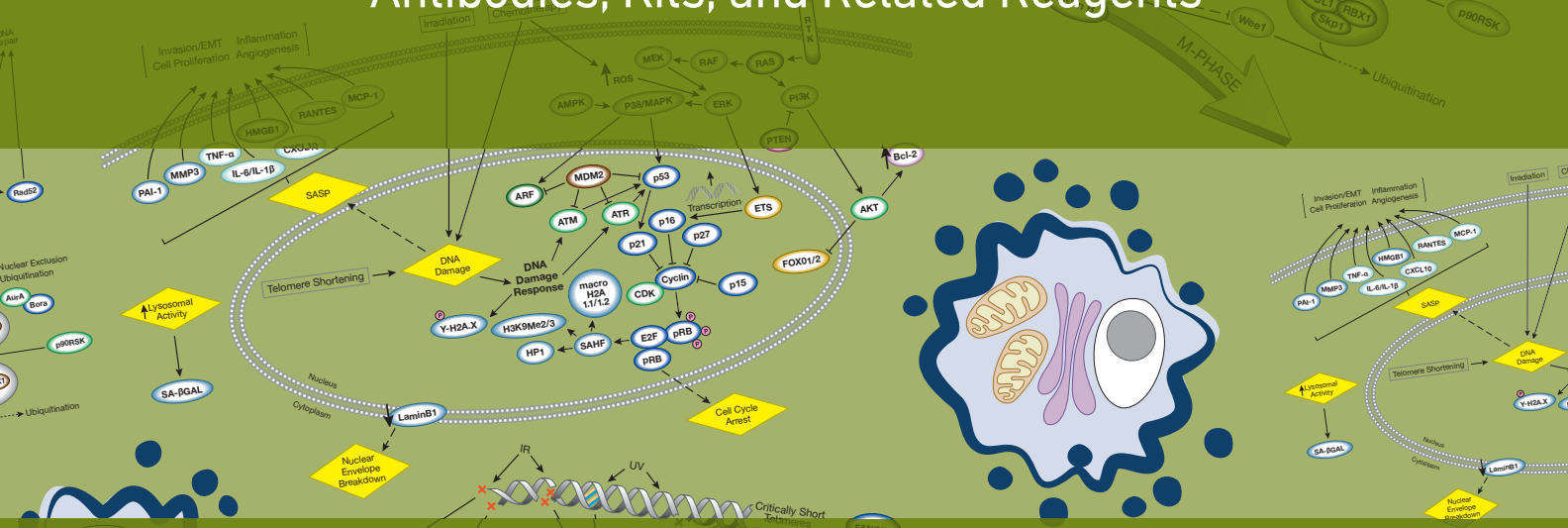
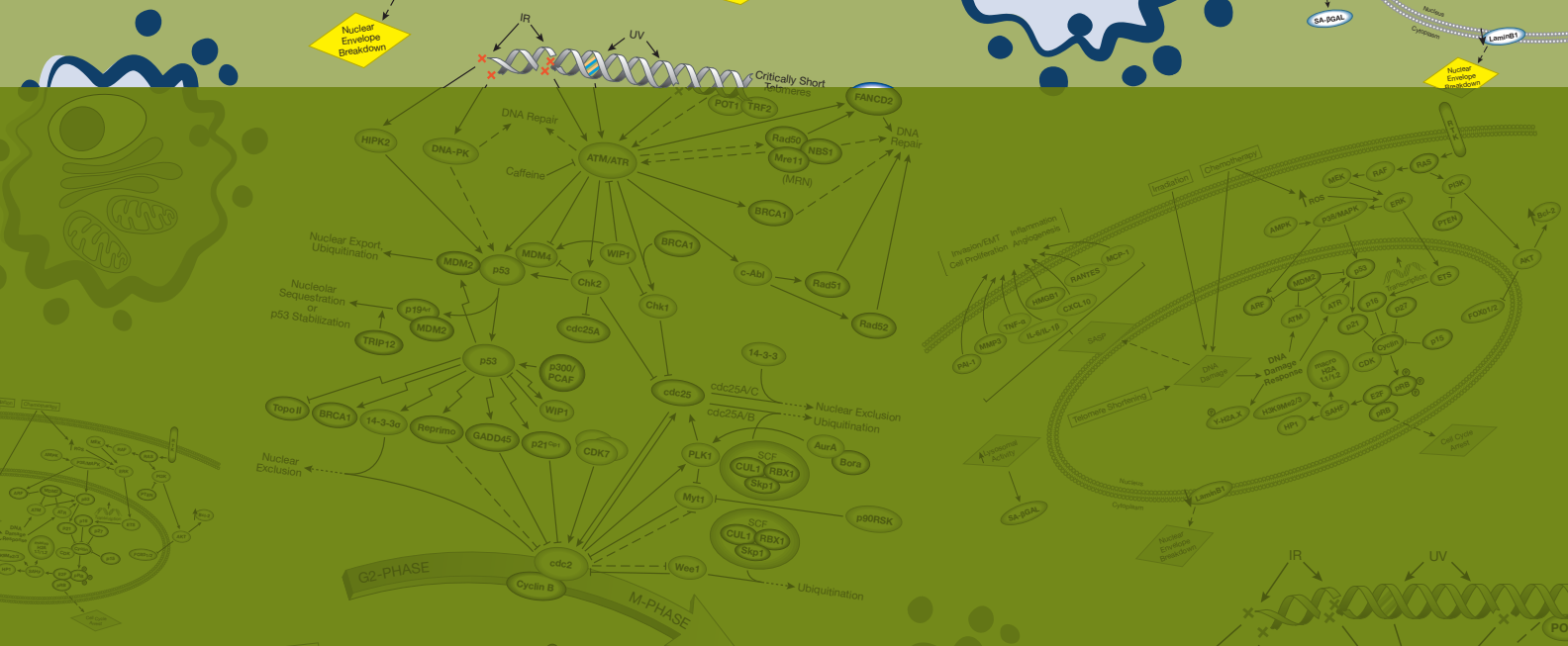
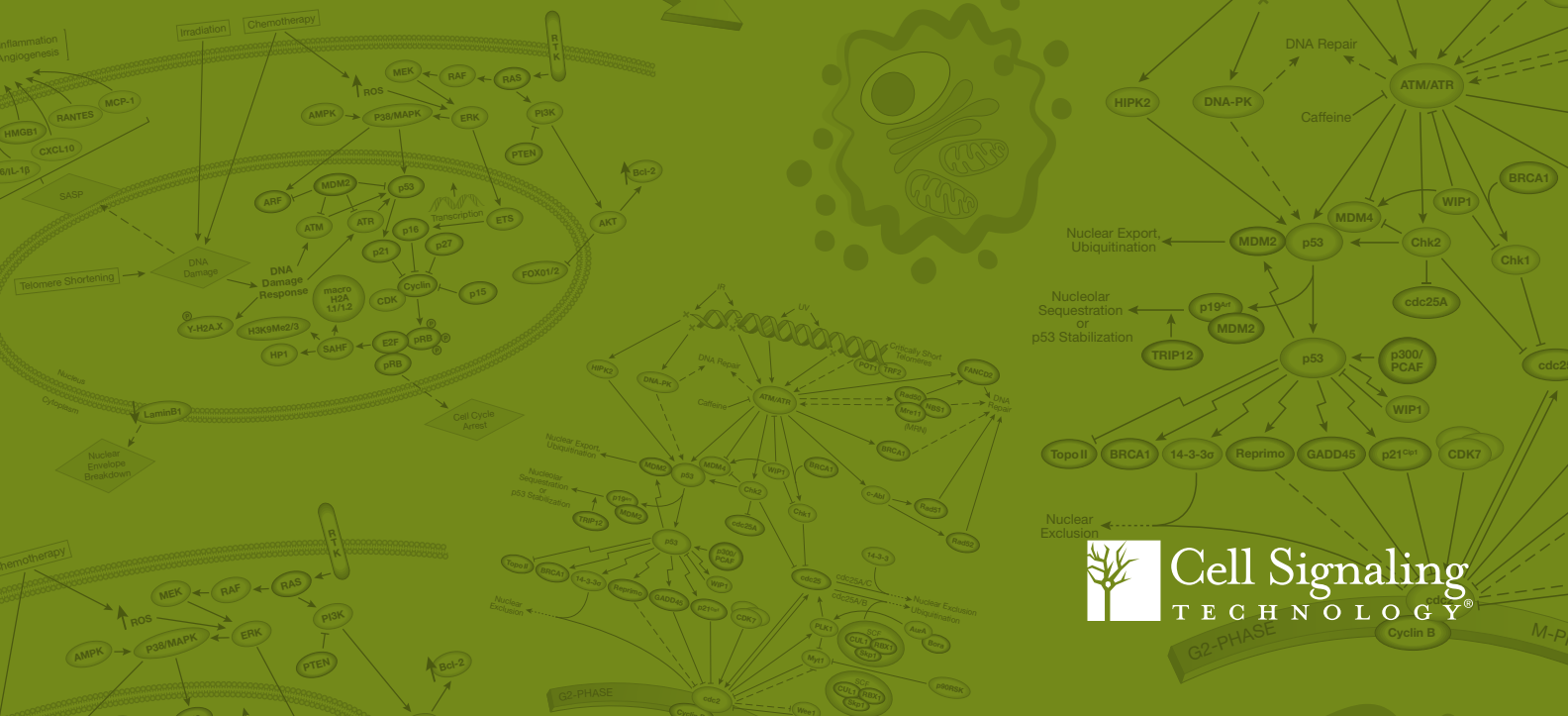
Cellular Senescence

Antibodies, Kits, and Related Reagents







Cell Signaling TECHNOLOGY®

What is senescence?

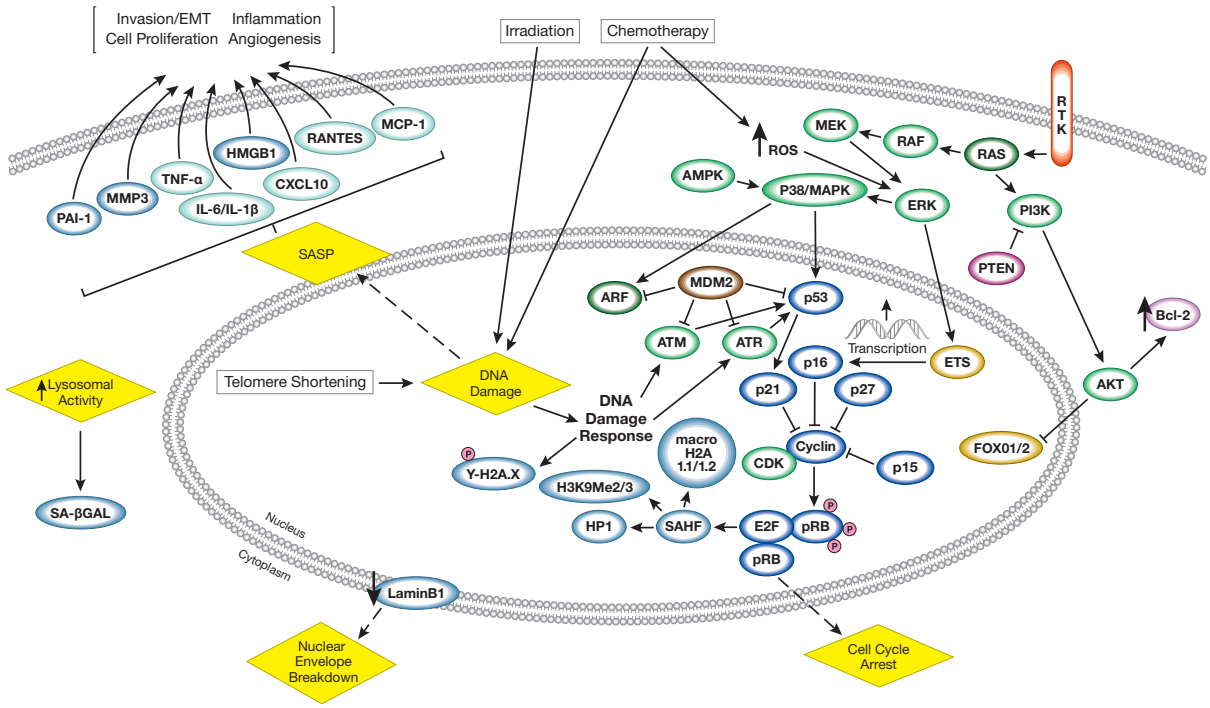
Cellular senescence refers to a state of stable cell cycle arrest in which proliferating cells become resistant to growth-promoting stimuli, typically in response to DNA damage. Senescence was first described by Leonard Hayflick upon the observation that human fetal fibroblasts eventually stopped dividing, but remained viable and metabolically active after prolonged time in culture. Senescent cells are distinct from both quiescent cells, which can reenter the cell cycle, and from terminally differentiated cells.

Identifying Senescent Cells

Although senescent cells share some identified characteristics, there is still no single assay or biomarker that can conclusively identify senescent cells in all cell types or under any conditions. That is because different senescent cells display different biomarkers of senescence. In addition, senescence biomarkers are not necessarily specific to senescent cells, as some markers are observed in apoptotic cells or quiescent cells, for example. Therefore, the identification of senescent cells depends on the observation of several biomarkers. These biomarkers can be detected using CST kits that test for senescence in different ways, providing an efficient way to identify senescent cells. Using a combination of these markers will provide a more comprehensive insight when evaluating the senescence status.

Contents

Senescence Signaling



WHY DOES SENESCENCE OCCUR?

Senescence typically occurs in response to damaging stimuli, including telomere shortening (replicative senescence), DNA damage (DNA damage-induced senescence), and oncogenic signaling (oncogene-induced senescence).

Understanding Replicative Senescence and Hayflick Limit

Replicative senescence refers to the phenomenon whereby normal nonmalignant cells stop dividing *in vitro*, after approximately fifty divisions, which has been termed the Hayflick limit. Replicative senescence is induced by telomere shortening. With each round of DNA replication, telomeres are progressively shortened, eventually reaching a critical length which prevents further replication, thereby halting cell division. Critically short, uncapped telomeres initiate a DNA damage response that triggers senescence.

DNA Damage-Induced Senescence

DNA damage triggers the DNA repair machinery, apoptosis, or senescence depending on the extent of damage and physiological context. Senescent cells are characterized by a persistent DNA damage response (DDR), including chronic ATM (Ataxia Telangiectasia mutated) and ATR (Ataxia Telangiectasia and Rad3 related) kinase signaling, which ultimately invokes cell cycle arrest and senescence through activation of the p53/p21 and p16/pRb pathways. Persistent DNA damage and subsequent senescence can also be induced by ionizing radiation, chemotherapeutics, genotoxic stress, and oxidative stress.

Oncogene-induced Senescence

Cellular senescence is induced in response to oncogenic signaling as a potent cell autonomous anti-cancer mechanism. Senescence occurring in cells with oncogenic signaling is a response intended to prevent their transformation to malignant cells. Oncogene-induced senescence (OIS) results from the hyperactivation of oncogenes like H-Ras or the inactivation of tumor suppressors such as PTEN. For example, expression of H-RASV12, an oncogenic form of the GTPase H-RAS, triggers OIS by inducing chronic p38 mitogen-activated protein kinase (p38 MAPK) signaling. Strong mitogenic signaling can also induce DNA damage via replication stress, which triggers the collapse of stalled replication forks.

TARGETING SENESCENCE TO TREAT DISEASES

Senescent cells accumulate with age and contribute to the normal aging process and age-related disorders, which include the degenerative diseases such as neurodegeneration, metabolic and cardiovascular diseases, as well as neoplastic diseases such as cancer. Senescence serves as a double-edged sword because it can stop the proliferation of damaged cells such as cancer cells, but it also promotes cell dysfunction. Senolytic therapies that intend to kill senescent cell using small molecules are currently being tested in humans in clinical trials for treatment of osteoarthritis and chronic kidney disease. The use of senolytics in chemotherapy patients may help prevent cancer relapse and alleviate some side effects. Senolytics can also extend lifespan and delay age-associated physical decline in normal mice, suggesting they may be effective in treating age-related disorders.

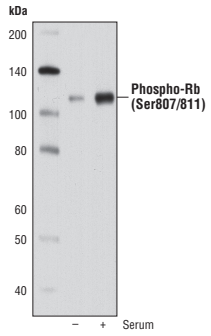
Features of Senescent Cells

Senescent cells display some features that distinguish them from other cells. Features of senescent cells include: stable cell cycle arrest, morphological and metabolic changes, adoption of the senescence-associated secretory phenotype (SASP), DNA damage and persistent DNA damage response (DDR), chromatin reorganization and altered gene expression, and telomere length and telomerase activity.

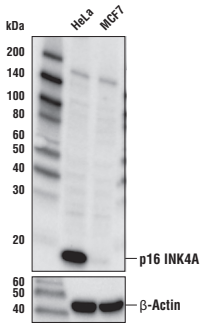
STABLE CELL CYCLE ARREST

Only cells with stable cell cycle arrest are considered senescent. Unlike a quiescent cell, a senescent cell will not reenter the cell cycle in response to any known physiological stimuli. Cell cycle arrest is mediated by the p53/p21CIP1 and p16INK4A/pRb tumor suppressor pathways. Examples of markers are cyclin dependent kinase inhibitors such as p16 INK4A or p21 Waf1/Cip. However, p16INK4A is also highly expressed in pRb-negative tumors and cell lines.

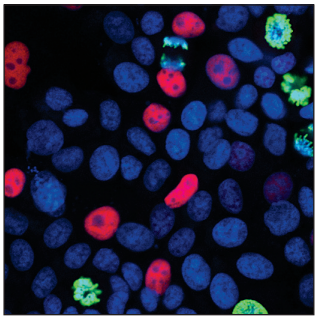
KEY TARGETS	ROLE IN SENESCENCE
p53	**Activation can trigger cell cycle arrest**
Rb	**Inhibition of phosphorylation triggers cell cycle arrest**
p16 INK4A	**Inhibits phosphorylation and inactivation of pRb**
p21 Waf1/Cip1	**Inhibits cyclin dependent kinases; downstream of p53**



Phospho-Rb (Ser807/811) (D20B12) XP® Rabbit mAb #8516: WB analysis of extracts from WI-38 cells, serum-starved for 3 days (-) or serum-starved for 3 days followed by treatment with 10% serum for 2 days (+), using #8516.



p16 INK4A (D7C1M) Rabbit mAb #80772: WB analysis of extracts from HeLa and MCF7 cells using p16 INK4A (D7C1M) Rabbit mAb (upper) or β-Actin (D6A8) Rabbit mAb #8457 (lower).

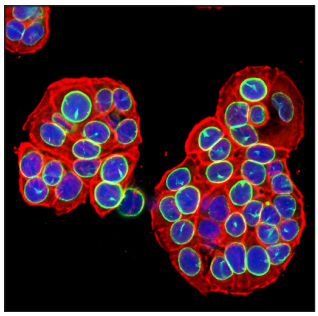


p21 Waf1/Cip1 (12D1) Rabbit mAb #2947: Confocal IF analysis of MCF7 cells using #2947 (red) and Phospho-Histone H3 (Ser10) (6G3) Mouse mAb #9706 (green). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).

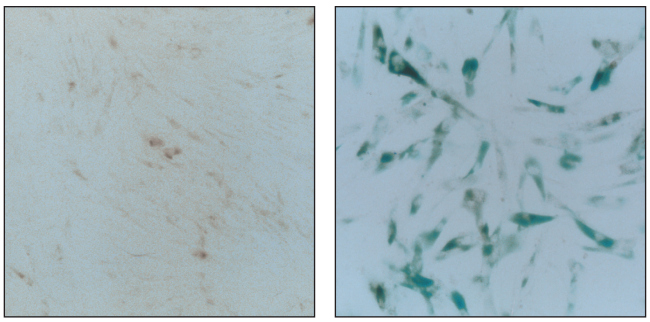
MORPHOLOGICAL AND METABOLIC CHANGES

Senescent cells typically have an enlarged size and flattened shape compared to their dividing cell counterparts. Senescent cells display extensive vacuolization and are sometimes multi-nucleated. In addition, disrupted nuclear envelope integrity is observed due to a loss of lamin B1 expression. Senescent cells accumulate dysfunctional mitochondria and display increased levels of reactive oxygen species (ROS). Increased lysosomal content and altered lysosomal activity is also observed, which is reflected by increased levels of β-galactosidase activity at pH 6.0, leading this to be widely adopted as a biomarker of cellular senescence.

KEY TARGETS	ROLE IN SENESCENCE
Lamin B1	**Expression reduced in senescent cells leading to disruption of nuclear envelope**
Senescence-associated β-galactosidase	**Increased activity at pH 6.0 in senescent cells**



Lamin B1 (119D5-F1) Mouse mAb #68591: Confocal IF analysis of HT-29 cells using #68591 (green) and β-Actin (13E5) Rabbit mAb (Alexa Fluor® 647 Conjugate) #8584 (red). Blue pseudocolor = Propidium Iodide (PI)/RNase Staining Solution #4087 (fluorescent DNA dye).



Senescence β-Galactosidase Staining Kit #9860: β-Galactosidase staining at pH 6 on normal WI-38 cells at population doubling 29 (left) and senescent WI-38 cells at population doubling 36 (right).

SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE (SASP)

Many senescent cells acquire a pro-inflammatory senescence-associated secretory phenotype (SASP) that mediates non-cell autonomous effects of senescence, both beneficial and deleterious. The SASP is comprised of a highly complex mixture of secreted cytokines, chemokines, growth factors, and proteases, with the precise composition varying markedly by cell and tissue context and the senescence-inducing stimulus. These secreted factors facilitate communication with neighboring cells and the immune system, which ultimately influences the fate of the senescent cell. For example, the SASP recruits immune cells to senescent cells, thereby facilitating their elimination, which serves a tumor suppressor function. Paradoxically, however, the SASP has been shown to promote tumor cell progression through secretion of factors that promote angiogenesis, extracellular matrix remodeling, or epithelial-mesenchymal transition (EMT). Additionally, chronic senescence-induced inflammation can induce systemic immunosuppression, potentially leading to the onset of diseases like cancer. This chronic inflammation may also drive tissue damage and degeneration associated with aging.

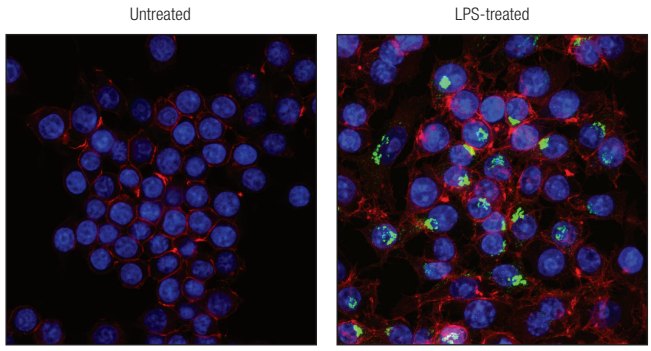
KEY SASP COMPONENTS

HMGB1 (High mobility group protein B1)
IL-6 (Interleukin 6)
TNF-α (Tumor necrosis factor α)
MMP3 (Matrix metalloproteinase-3)
IL-1β
RANTES
CXCL10
PAI-1
TNF-α
MCP-1

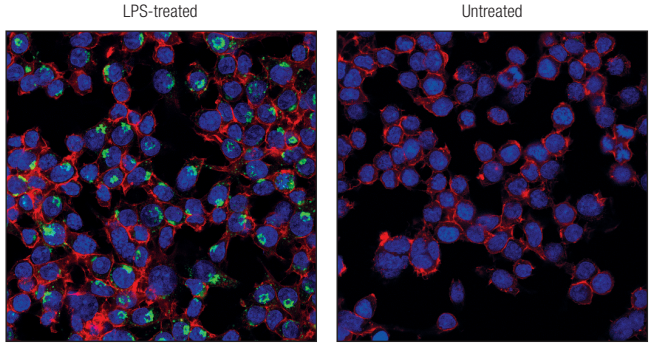
Senescence Associated Secretory Phenotype (SASP) Antibody Sampler Kit #38461

Senescence Associated Secretory Phenotype (SASP) Antibody Sampler Kit provides an economical means of detecting multiple components of the SASP. The kit includes enough antibody to perform two western blot experiments with each primary antibody.

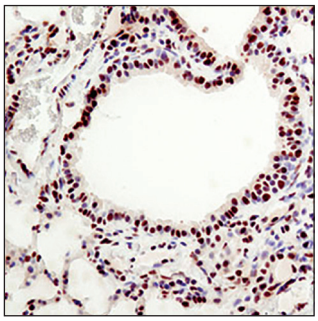
Define the specific SASP factors expressed



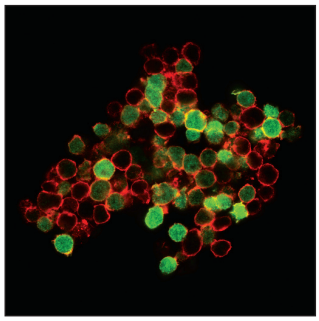
IL-6 (D5W4V) XP® Rabbit mAb (Mouse Specific) #12912: Confocal IF analysis of Raw 264.7 cells, untreated (left) or treated with LPS (100 ng/ml, 6 hr; right), using #12912 (green). Actin filaments were labeled with DY-554 phalloidin (red). Blue pseudocolor= DRAQ5® #4084 (fluorescent DNA dye).



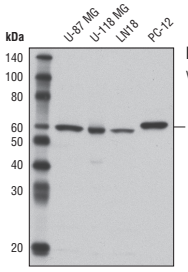
TNF-α (D2D4) XP® Rabbit mAb (Mouse Specific) #11948: Confocal IF analysis of Raw 264.7 cells, treated with LPS (100 ng/mL, 6 hr; left) or untreated (right), using #11948 (green). Actin filaments were labeled with DY-554 phalloidin (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



HMGB1 (D3E5) Rabbit mAb #6893: IHC analysis of paraffin-embedded mouse lung using #6893.



IL-1β (D3U3E) Rabbit mAb #12703: Confocal IF analysis of LPS-treated THP-1 cells (500 ng/ml, 2 hr), using #12703 (green). Actin filaments were labeled with DY-554 phalloidin (red).



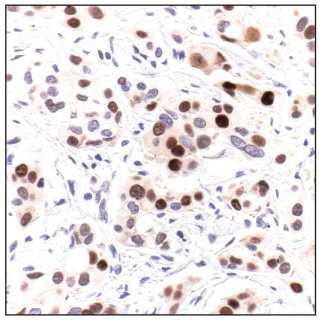
MMP-3 (D7F5B) Rabbit mAb #14351: WB analysis of extracts from various cell lines using #14351.

Features of Senescent Cells

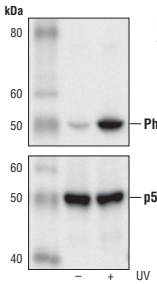
DNA DAMAGE AND PERSISTENT DNA DAMAGE RESPONSE (DDR)

DNA damage, such as DNA double strand breaks, is a prominent feature of senescence. Senescent cells display a persistent DNA damage response (DDR) that ultimately triggers cell cycle arrest. Senescent cells contain nuclear foci called DNA segments with chromatin alterations reinforcing senescence (DNA-SCARS), which associate with PML nuclear bodies and accumulate DDR proteins such as activated p53, ATR, and ATM. DNA-SCARS that occur at uncapped telomeres are called telomere dysfunction-induced foci (TIF). Another indicator of DNA damage is γ-H2A.X, which is the phosphorylated form of H2A.X, a variant histone required for checkpoint-mediated cell cycle arrest and DNA repair following double-stranded DNA breaks. DNA damage, caused by ionizing radiation, UV light, or radiomimetic agents, results in rapid phosphorylation of H2A.X at Ser139.

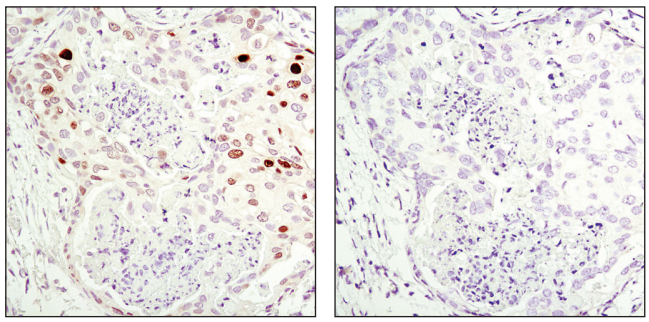
KEY TARGETS	ROLE IN SENESCENCE
Phospho-Histone H2A.X (Ser139)	**In response to DNA damage, histone H2A.X protein is phosphorylated at Ser139 by kinases such as ATM and ATR, leading to recruitment of other DDR proteins at sites of DNA damage**
Rad51	**Rad51 recombinase is a mediator of homologous recombination repair, and a marker of DNA damage**
p53	**Tumor suppressor protein activated by Chk1- or Chk2-mediated phosphorylation in response to DNA damage**
Phospho-p53	**Activation of p53 by phosphorylation triggers induction of p21 Waf1/Cip1 expression, which leads to downstream arrest of the cell cycle**
p21 Waf1/Cip1	**Tumor suppressor protein induced following p53 activation, which inhibits cyclin dependent kinases leading to cell cycle arrest**
53BP1	**53BP1 is a DDR protein that promotes repair of double stranded DNA breaks**



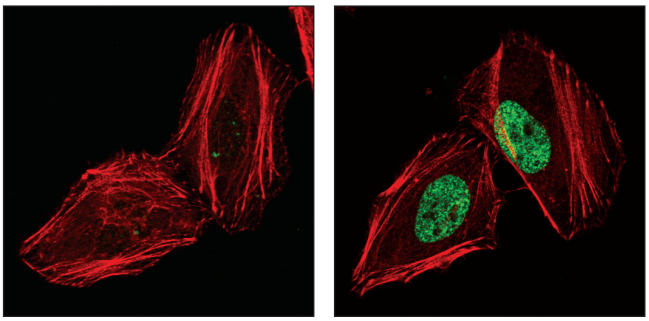
p53 (7F5) Rabbit mAb #2527: IHC analysis of paraffin-embedded human breast carcinoma, using #2527.



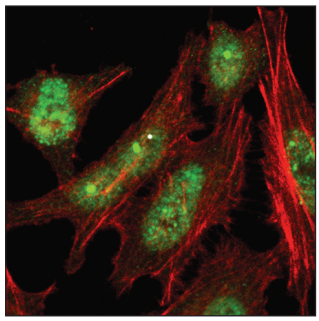
Phospho-p53 (Ser15) (16G8) Mouse mAb #9286: WB analysis of extracts from HT29 cells, untreated or UV-treated (100 mJ/cm^2, 1 hr), using #9286 (upper) or p53 (DO-7) Mouse mAb #48818 (lower).



p21 Waf1/Cip1 (12D1) Rabbit mAb #2947: IHC analysis of paraffin-embedded human breast carcinoma using #2947 in the presence of control peptide (left) or antigen-specific peptide (right).

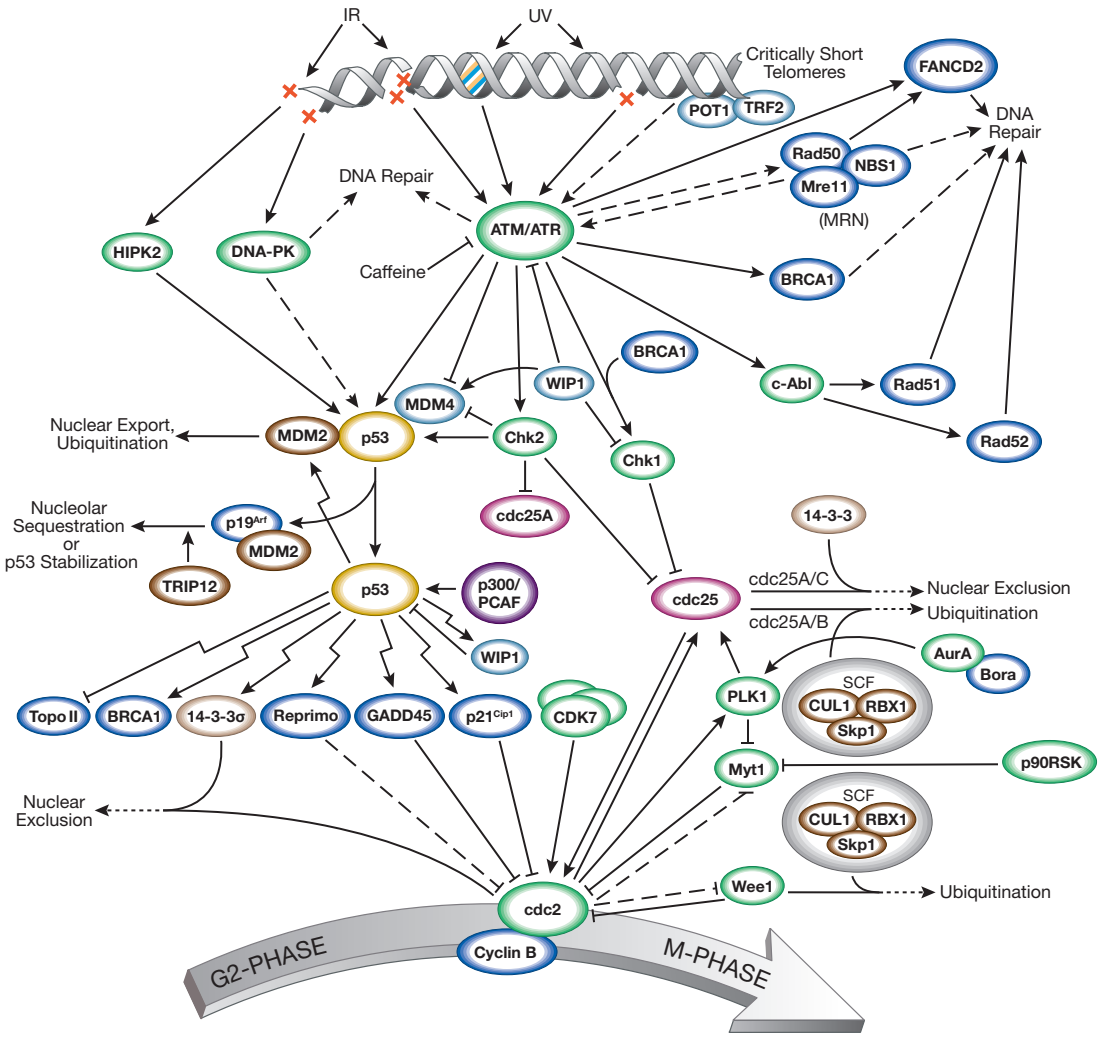


Phospho-Histone H2A.X (Ser139) (20E3) Rabbit mAb #9718: Confocal IF analysis of HeLa cells, untreated (left) or UV-treated (right), using #9718 (green). Actin filaments have been labeled with DY-554 phalloidin (red).



53BP1 Antibody #4937: Confocal IF analysis of HeLa cells using #4937 (green). Actin filaments have been labeled with Alexa Fluor® 555 phalloidin (red).

G2/M DNA DAMAGE CHECKPOINT



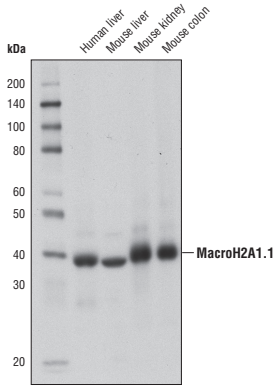
The G2/M DNA damage checkpoint serves to prevent the cell from entering mitosis (M-phase) with genomic DNA damage. Specifically, the activity of the Cyclin B-cdc2 (CDK1) complex is pivotal in regulating the G2-phase transition wherein cdc2 is maintained in an inactive state by the tyrosine kinases Wee1 and Myt1. It is thought that coordinated action of the kinase Aurora A and the cofactor Bora activate PLK1 as cells approach the M-phase, which in turn activates the phosphatase cdc25 and downstream cdc2 activity, hence establishing a feedback amplification loop that efficiently drives the cell into mitosis. Importantly, DNA damage cues activate the sensory DNA-PK/ATM/ATR kinases, which relay two parallel cascades that ultimately serve to inactivate the Cyclin B-cdc2 complex. The first cascade rapidly inhibits progression into mitosis: the Chk kinases phosphory- late and inactivate cdc25, which prevents activation of cdc2. The slower second parallel cascade involves phosphorylation of p53 and allows for its dissociation from MDM2 and MDM4 (MdmX), which activates DNA binding and transcriptional regulatory activity, respectively. The transcriptional ability of p53 is further augmented through acetylation by the co-activator complex p300/PCAF. The second cascade constitutes the p53 downstream-regulated genes including: 14-3-3, which binds to the phosphorylated Cyclin B-cdc2 complex and exports it from the nucleus; GADD45, which binds to and dissociates the Cyclin B-cdc2 complex; and p21 Waf1/Cip1, an inhibitor of a subset of the cyclin-dependent kinases including cdc2. Recent data suggest an important role for the p53-regulated WIP1 phosphatase that acts as a critical dampener of DNA damage signaling in cancer. In human cancer, researchers have found p53 to be commonly mutated, indicating that this checkpoint is a critical barrier to tumor formation. In addition, sporadic and familial mutations in the DNA-repair proteins such as the BRCA-family, ATM, and the Fanconi Anemia proteins further highlight this as a key tumor suppressor checkpoint.

Features of Senescent Cells

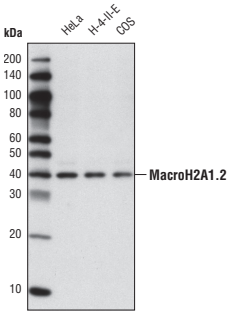
CHROMATIN REORGANIZATION AND ALTERED GENE EXPRESSION

A hallmark feature of senescent cells is extensive chromatin reorganization, most notably the formation of senescence-associated heterochromatin foci (SAHF). These sites of facultative heterochromatin play a role in silencing genes that promote proliferation, including E2F target genes like cyclin A. Senescent cells typically contain 30-50 SAHF, which are characterized by bright DAPI staining and macroH2A, heterochromatin protein 1 (HP1), and lysine 9 di-or-tri-methylated histone H3 (H3K9Me2/3) immunoreactivity. Although SAHF is frequently observed during senescence, some cells undergo senescence without forming SAHF.

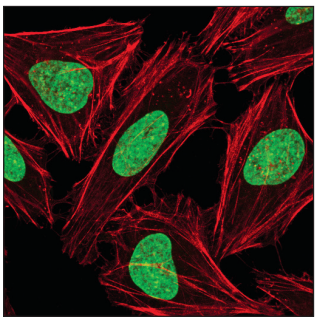
KEY TARGETS	ROLE IN SENESCENCE
macroH2A1.1	**macroH2A1 isoform; marker of SAHF**
macroH2A1.2	
HP1	**Marker of SAHF**
H3K9Me2/3	



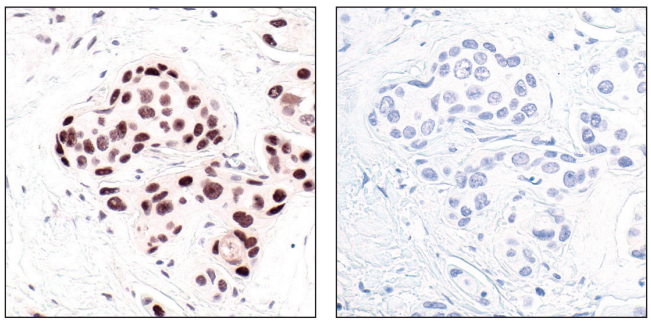
MacroH2A1.1 (D5F6N) Rabbit mAb #12455: WB analysis of extracts from various tissues using #12455.



MacroH2A1.2 Antibody #4827: WB analysis of extracts from HeLa, H-4-II-E, and COS cells using #4827.



Di/Tri-Methyl-Histone H3 (Lys9) (6F12) Mouse mAb #5327: Confocal IF analysis of HeLa cells using #5327 (green). Actin filaments have been labeled with DY-554 phalloidin (red).

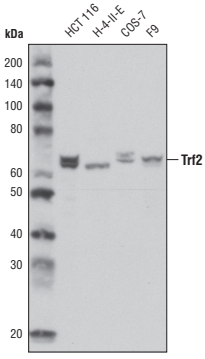


HP1α Antibody #2616: IHC analysis of paraffin-embedded human breast carcinoma, using #2616 in the presence of control peptide (left) or HP1 alpha blocking peptide #1004 (right).

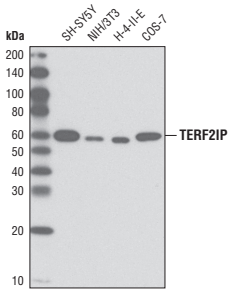
TELOMERES AND THEIR ROLE IN SENESCENCE

Telomeres are the repetitive nucleotide sequences and associated proteins at the ends of chromosomes that serve as protective caps against chromosomal degradation and end-to-end fusion. Telomeres are comprised of hundreds to thousands of short GT-rich tandem repeat sequences, followed by a single-stranded GT-rich overhang. Telomere-binding proteins constituting the shelterin complex bind the repeat sequence and promote a T-loop structure, which caps the chromosome end. The shelterin complex is comprised of telomere repeat factor 1 (TRF1), telomere repeat factor 2 (TRF2), telomeric repeat-binding factor 2-interacting protein (TERF2IP, also known as RAP1), protection of telomere 1 (POT1), TRF1- and TRF2-interacting nuclear protein 2 (TIN2), and the TIN2 binding protein TPP1.

Telomeric sequences cannot be completely replicated by DNA polymerase, which leads to their progressive truncation in most somatic cells. Transformed cells, stem cells, and germ cells express telomerase, a ribonucleoprotein complex that synthesizes telomeric end sequences *de novo*. The telomerase complex is comprised of telomerase reverse transcriptase (TERT), telomerase RNA (TERC), and dyskerin (DKC1) . Because telomere length is maintained in telomerase expressing cells, they are able to continuously proliferate without achieving replicative senescence.



TRF2 (D1Y5D) Rabbit mAb #13136: WB analysis of extracts from various cell lines using #13136.

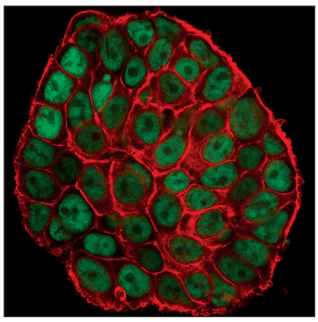


TERF2IP (D9H4) Rabbit mAb #5433: WB analysis of extracts from various cell lines using #5433.

Workflows and Key Targets

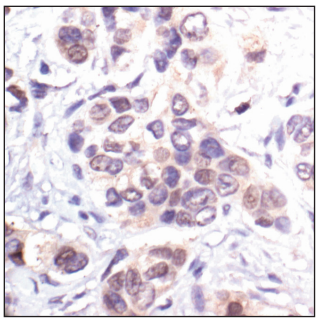
DETECTING DIFFERENT TYPES OF SENESCENCE

DNA Damage Response



Phospho-p53 (Ser15) (16G8) Mouse mAb #9286: Confocal IF analysis of HT-29 cells, untreated (left) or UV-treated (right), using #9286 (green). Actin filaments have been labeled with Alexa Fluor® 555 phalloidin (red).

Cell Cycle Arrest



p21 Waf1/Cip1 (DCS60) Mouse mAb #2946: IHC analysis of paraffin-embedded human breast carcinoma, showing nuclear and cytoplasmic localization, using #2946.

SUMMARY OF SENESCENCE TARGETS

KEY TARGETS	ROLE IN SENESCENCE
Lamin B1 Senescence-associated β-galactosidase	**Morphological Changes**
Rb / phospho-Rb p16 INK4A p53 / phospho-p53 p21 Waf1/Cip1	**Markers of Cell Cycle Arrest**
Phospho-Histone H2A.X (Ser139) 53BP1 Rad51	**Markers of DNA Damage**
HMGB1 (High mobility group protein B1) IL-6 (Interleukin 6) TNF-α (Tumor necrosis factor α) MMP3 (Matrix metalloproteinase-3) IL-1β RANTES CXCL10 PAI-1 TNF-α MCP-1	**SASP components**
macroH2A1.1 macroH2A1.2 HP1 H3K9Me2/3	**Markers of Senescence-associated heterochromatin foci (SAHF)**

WORKFLOW TO IDENTIFY SENESCENCE CELLS

Screening for senescence

Senescence-associated-β-gal and/or
Lipofuscin (SBB/GL13)

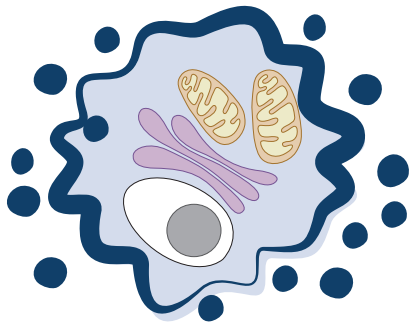
Verification with additional markers (co-staining)

- ↑ $p16^{INK4A}$
- ↑ $p21^{WAF/Cip1}$
- ↓ Proliferation markers
- ↓ Lamin B1

Markers for specific types of senescence

SASP
DNA damage and DDR
PI3K/FOXO/mTOR

Senescence detection and phenotype



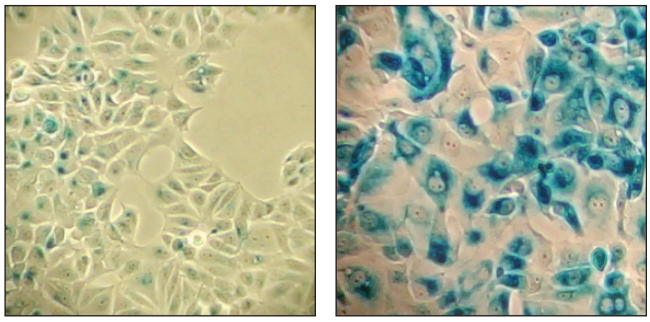
adapted from Gorgoulis, V. et al, (2019) *Cell* 179(4):813-827.

Tools to Detect Senescent Cells

STAINING KIT

The Senescence β-Galactosidase Staining Kit is designed to conveniently provide reagents needed to detect β-galactosidase activity at pH 6.0, a known characteristic of senescent cells. Papers have been published using this kit in both cells and frozen tissue.

β-galactosidase activity staining



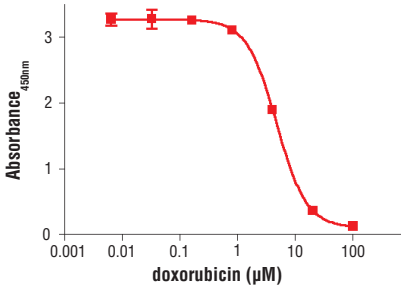
Senescence β-Galactosidase Staining Kit #9860: β-Galactosidase staining at pH 6.0 on MCF-7 cells untreated (left) and senescent MCF-7 cells treated with etoposide #2200 (12.5 µM, 24 hr) and allowed to recover for 4 days (right).

BRDU CELL PROLIFERATION ASSAY KITS

BrdU Cell Proliferation Assays Kits, are used to detect proliferating cells, the absence of which is a feature of senescence.

BrdU Cell Proliferation Assay Kit #6813

BrdU Cell Proliferation Chemiluminescent Assay Kit #5492



BrdU Cell Proliferation Assay Kit #6813: Jurkat cells were seeded at 4x10^4 cells/well in a 96-well plate and incubated overnight. Cells were then treated with various concentrations of doxorubicin for 2 hr. Finally, 10 µM BrdU was added to the plate and cells were incubated for 4 hr.

It is important to note that not all senescent cells display all biomarkers of senescence. In addition, senescence biomarkers are not necessarily specific to senescent cells, as some markers are observed in apoptotic cells or quiescent cells. Therefore, there is currently no universal marker of senescence. Investigators must assess several senescence-associated markers in aggregate to provide evidence of a senescent phenotype as the markers that are expressed in senescent cells vary depending on the senescence stimulus, cell type, and timing.

SAMPLER KITS

The sampler kit provides researchers with an economical means to investigate various aspects of cellular signaling.

Senescence Marker Antibody Sampler Kit #56062

	PRODUCT INCLUDES	APPLICATION	REACTIVITY
92803	p16 INK4A (D3W8G) Rabbit mAb	WB, IP	H
2947	p21 Waf1/Cip1 (12D1) Rabbit mAb	WB, IP, IHC-P, IF-IC, F	H, Mk
9718	Phospho-Histone H2A.X (Ser139) (20E3) Rabbit mAb	WB, IHC-P, IF-IC, F	H, M, R, Mk
13435	Lamin B1 (D9V6H) Rabbit mAb	WB, IP	H, M, R
6893	HMGB1 (D3E5) Rabbit mAb	WB, IHC-P	H, M, R, Mk
12153	IL-6 (D3K2N) Rabbit mAb	WB, IP	H
6945	TNF-α (D5G9) Rabbit mAb	WB, IP	H
14351	MMP3 (D7F5B) Rabbit mAb	WB	H, R
7074	Anti-Rabbit IgG, HRP-linked Antibody	WB	

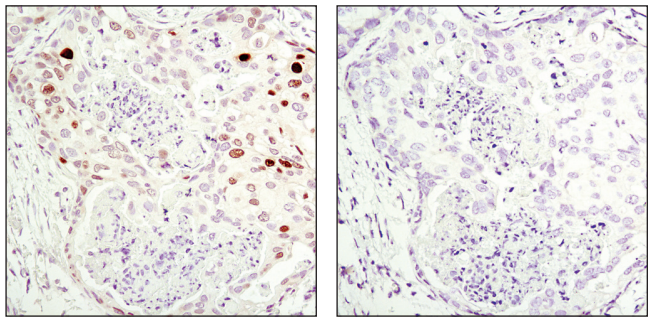
Senescence Associated Secretory Phenotype (SASP) Antibody Sampler Kit #38461

	PRODUCT INCLUDES	APPLICATION	REACTIVITY
12703	IL-1-β (D3U3E) Rabbit mAb	WB, IF-IC, F	H
2987	RANTES (R40) Rabbit Ab	WB	H
14969	CXCL10 (D5L5L) Rabbit mAb	WB	H
11907	PAI-1 (D9C4) Rabbit mAb	WB	H, Mk, B
12153	IL-6 (D3K2N) Rabbit mAb	WB, IP	H
6945	TNF-α (D5G9) Rabbit mAb	WB, IP	H
14351	MMP3 (D7F5B) Rabbit mAb	WB	H, R
39091	MCP-1 Antibody (Carboxy-terminal Antigen)	WB, IP	H
7074	Anti-Rabbit IgG, HRP-linked Antibody	WB	

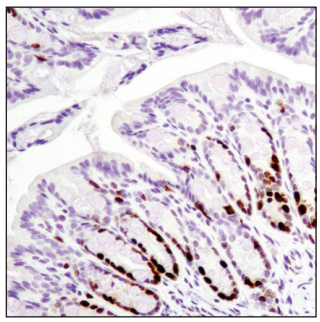
CST Products to Facilitate Your Senescence Research

	ANTIBODIES	APPLICATION	REACTIVITY
88439	53BP1 (E7N5D) XP® Rabbit mAb	WB, IHC-P, IF-IC	H
4187	AMPKγ1 Antibody	WB	H, Mk
2873	ATM (D2E2) Rabbit mAb	WB	H M
13050	Phospho-ATM (Ser1981) (D25E5) Rabbit mAb	WB, F	H (Mk)
15071	Bcl-2 (124) Mouse mAb	WB, IP, IHC-P, F	H
2764	Bcl-xL (54H6) Rabbit mAb	WB, IP, IHC-P, IF-IC, F	H M R Mk
13440	BRD4 (E2A7X) Rabbit mAb	WB, IP, ChIP	H (B) (Dg) (Pg)
4915	CD54/ICAM-1 Antibody	WB, IHC-P	H
14969	CXCL10 (D5L5L) Rabbit mAb	WB	H
67138	DPP4/CD26 (D6D8K) Rabbit mAb	WB, IP, IF-IC	H
40134	DPP4/CD26 (D6D8K) Rabbit mAb (IHC Formulated)	IHC-P	H
5246	Ezh2 (D2C9) XP® Rabbit mAb	WB, IP, IHC-P, IF-F, IF-IC, F, ChIP, ChIP-seq	H, M, R, Mk
27198	β-Galactosidase (E2U2I) Rabbit mAb	WB, IF-IC	H, M, R, Hm, Mk
9718	Phospho-Histone H2A.X (Ser139) (20E3) Rabbit mAb	WB, IHC-P, IF-IC, F	H, M, R, Mk
4658	Di-Methyl-Histone H3 (Lys9) (D85B4) XP® Rabbit mAb	WB, IP, IF-IC, F, ChIP	H, M, R, Mk, (Dm, X, Z, B, Pg, Sc, Ce)
9753	Di-Methyl-Histone H3 (Lys9) Antibody	WB, IP, ChIP	H, M, R, Mk, Dm
5327	Di/Tri-Methyl-Histone H3 (Lys9) (6F12) Mouse mAb	WB, IP, IF-IC, ChIP	H, M, R, Mk, (Dm, Z, Sc)
6893	HMGB1 (D3E5) Rabbit mAb	WB, IHC-P	H, M, R, Mk, (C, B, Hr)
2616	HP1α Antibody	WB, IP, IHC-P, IF-IC, F, ChIP	H, M, R, Mk, (B)
8676	HP1β (D2F2) XP® Rabbit mAb	WB, IP, IF-IC, ChIP, ChIP-seq	H, M,R, Mk, (Hm, B, GP)
2619	HP1γ Antibody	WB, IP, IF-IC, F	H, M, R, Mk
50794	IL-1α (D4F3S) Rabbit mAb (Mouse Specific)	WB, IP, F	M
12703	IL-1β (D3U3E) Rabbit mAb	WB, IF-IC, F	H
12242	IL-1β (3A6) Mouse mAb	WB, IHC-P	H, M
12153	IL-6 (D3K2N) Rabbit mAb	WB, IP	H
12912	IL-6 (D5W4V) XP® Rabbit mAb (Mouse Specific)	WB, IP, IF-IC, F	M
9129	Ki-67 (D3B5) Rabbit mAb	IF-F, IF-IC, F	H, M ,R
12202	Ki-67 (D3B5) Rabbit mAb (Mouse Preferred; IHC Formulated)	IHC-P	M
9449	Ki-67 (8D5) Mouse mAb	IHC-P, IF-IC, F	H
13435	Lamin B1 (D9V6H) Rabbit mAb	WB, IP	H, M, R, (B, Dg, Pg)
68591	Lamin B1 (119D5-F1) Mouse mAb	IF-IC	H
2029	MCP-1 Antibody (Mouse Specific)	WB	M
14351	MMP-3 (D7F5B) Rabbit mAb	WB	H, R
74560	p14 ARF (E3X6D) Rabbit mAb	WB, IHC-Bond, IHC-P, IF-IC, F	H
92803	p16 INK4A (D3W8G) Rabbit mAb	WB, IP	H
80772	p16 INK4A (D7C1M) Rabbit mAb	WB, IP, F	H

	ANTIBODIES	APPLICATION	REACTIVITY
2947	p21 Waf1/Cip1 (12D1) Rabbit mAb	WB, IP, IHC-P, IF-IC, F	H, Mk, (Dg)
64016	p21 Waf1/Cip1 Antibody (Mouse Preferred)	WB, IP	M
3686	p27 Kip1 (D69C12) XP® Rabbit mAb	WB, IP, IF-IC, F	H, R, Mk
2527	p53 (7F5) Rabbit mAb	WB, IHC-P, IF-IC, F, ChIP	H, Mk
2524	p53 (1C12) Mouse mAb	WB, IP, IF-IC, F, ChIP	H, M, R, Hm, Mk
9284	Phospho-p53 (Ser15) Antibody	WB, IP, ChIP	H, M, R, M,k (Mi, B, Pg)
9286	Phospho-p53 (Ser15) (16G8) Mouse mAb	WB, IF-IC, F	H
11907	PAI-1 (D9C4) Rabbit mAb	WB	H, Mk, B
2988	RANTES (P20) Antibody	WB	H, (Mk)
2989	RANTES Antibody (Rodent Specific)	WB, IP	M, (R)
9313	Rb (D20) Rabbit mAb	WB, IP, ChIP	H, M, Mk
9309	Rb (4H1) Mouse mAb	WB, IP, IHC-P, IF-IC, F, ChIP	H, Mk, B, Pg
8180	Phospho-Rb (Ser780) (D59B7) Rabbit mAb	WB, IP	H, M, R, Mk
8516	Phospho-Rb (Ser807/811) (D20B12) XP® Rabbit mAb	WB, IP, IHC-P, IF-IC, F	H, M, R, Mk
8184	TNF-α (D1G2) Rabbit mAb (IF/Flow Preferred)	WB, IP, IF-IC, F	H
11948	TNF-α (D2D4) XP® Rabbit mAb (Mouse Specific)	WB, IP, IF-IC, F	M



p21 Waf1/Cip1 (12D1) Rabbit mAb #2947: IHC analysis of paraffin-embedded human breast carcinoma using #2947 in the presence of control peptide (left) or antigen-specific peptide (right).



Ki-67 (D3B5) Rabbit mAb (Mouse Preferred; IHC Formulated) #12202: IHC analysis of paraffin-embedded mouse colon using #12202.

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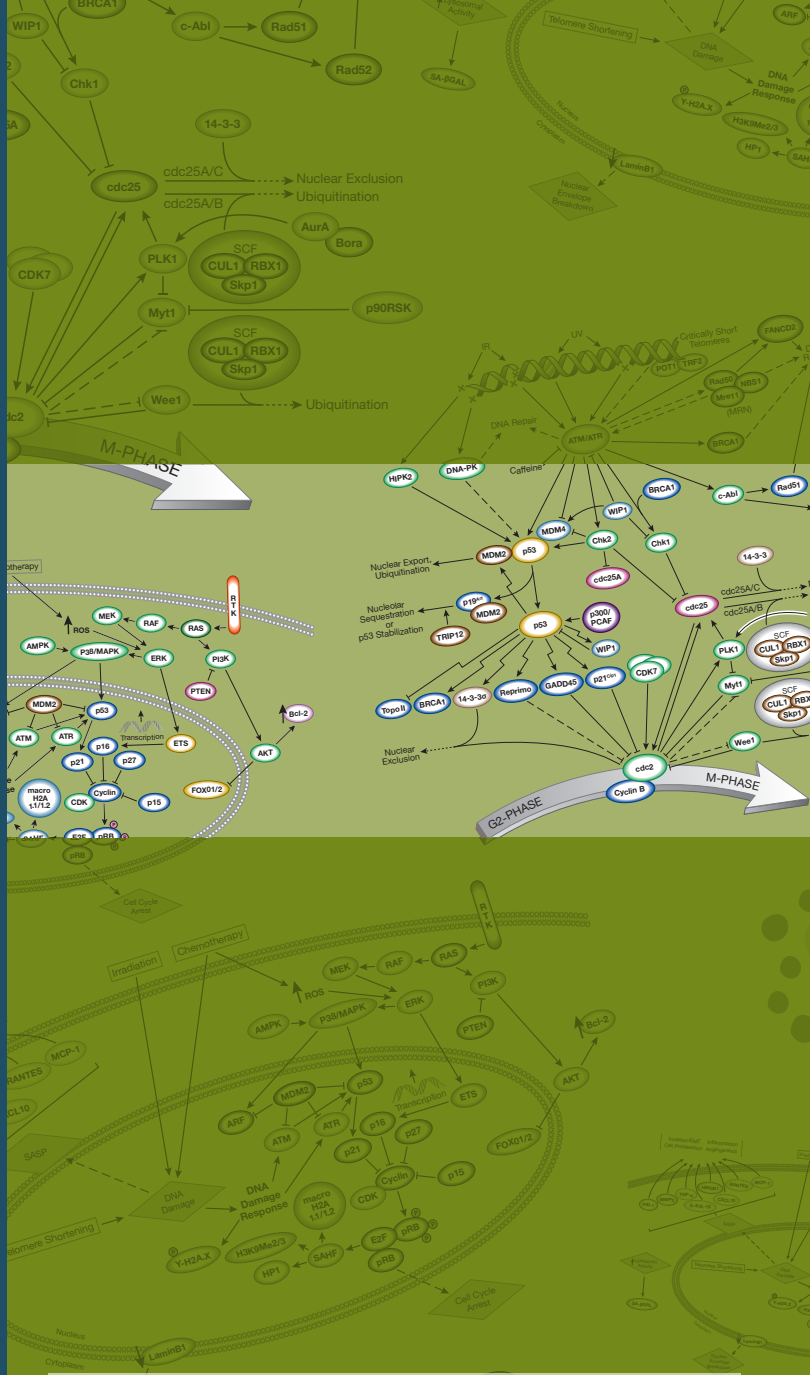

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