EuroClone®

Hallmarks of Neurodegeneration

Identifying Underlying Biological Processes

Cell Signaling TECHNOLOGY®

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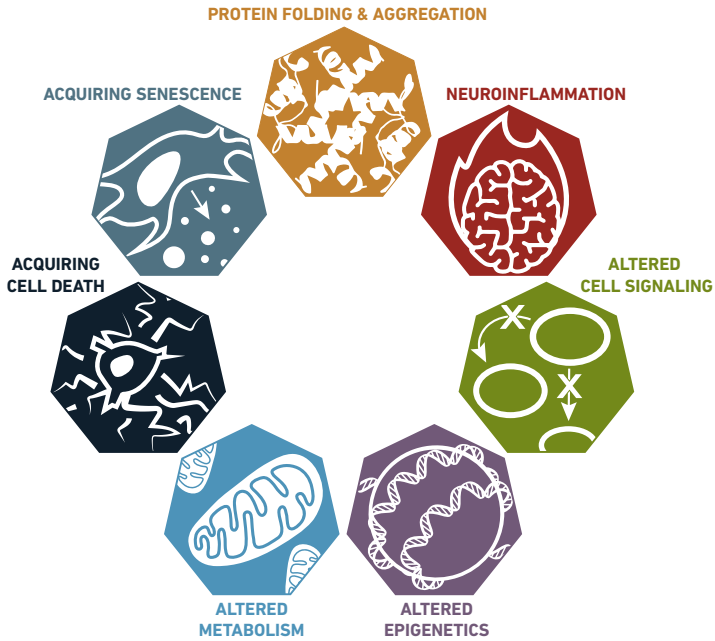
Introduction

Neurodegenerative diseases are characterized by a loss of neuronal structure and function that leads to problems with movement (ataxis) or mental function (dementia). These changes occur due to genetic mutations or protein folding disorders that can accumulate with age. While pathophysiologies like amyloid plaques are well documented, many of the cellular processes that drive neurodegeneration have yet to be fully elucidated. Defects in these key processes may be shared among different neurogenerative diseases, making it likely that new therapies targeting one process may alleviate the progression of many conditions.

We've put together a starter's guide on the cellular mechanisms that drive neurodegeneration in diseases such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, and Huntington's disease. Wondering how to identify the many different cell types that make up the central nervous system (CNS)? We also have a Cell Type Marker guide on page 8.



DRIVERS OF NEURODEGENERATION:

Protein Folding and Aggregation

One hallmark of many neurodegenerative diseases is the accumulation of unfolded or misfolded proteins that lead to neurofibrillary tangles and plaques that cause neuronal cell cytotoxicity. There is increasing interest in the field on understanding the mechanisms required for the production and processing of proteins known to form these aggregates, as these protein aggregates are associated with Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. Some challenges to developing new therapies that target the protein aggregate formation include an incomplete knowledge of the mechanisms of action as well as a lack of biomarkers to diagnose conditions early and to monitor disease progression and therapeutic response. Interested in better understanding protein folding and aggregation?

Start with These Targets

β-amyloid

β-amyloid (Aβ) is a peptide that is the main component of the amyloid plaques observed in the brains of patients with Alzheimer's disease. The peptides are formed when the amyloid precursor protein (APP) is cleaved by β-secretase and γ-secretase.

β-Amyloid (D54D2) XP® Rabbit mAb #8243 – W, IP, **IF-P**

Phospho-Tau (Thr205)

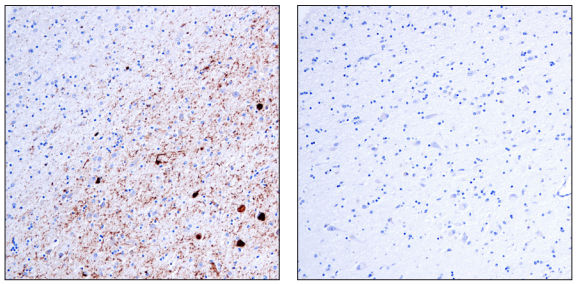
Under normal cellular conditions, Tau promotes and stabilizes microtubule assembly, especially in axons. Phosphorylation of Tau (Thr205) is well characterized in neurofibrillary tangles, with low levels in earlier stages and significantly higher levels in later stages of Alzheimer's disease.

Phospho-Tau (Thr205) (E7D3E) Rabbit mAb #49561 – W, IP, **IHC-P**, IF-F

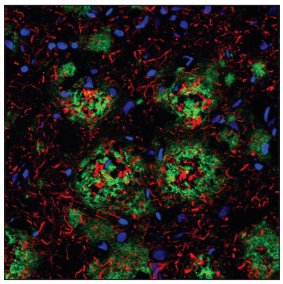
α/β-synuclein

Interest in α/β-synuclein began when mutations were observed in several families with autosomal-dominant Parkinson's disease. α/β-synuclein may regulate membrane stability and/or turnover; however, its normal cellular function has not been conclusively determined. α/β-synuclein mutations are associated with early onset familial Parkinson's disease.

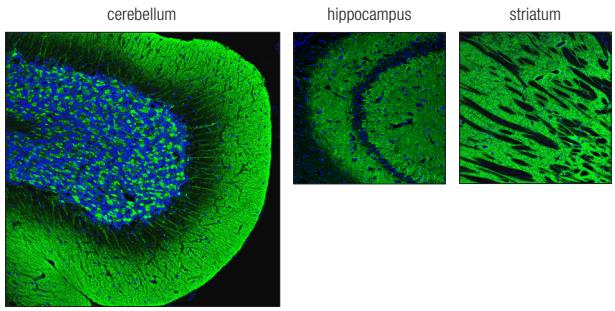
α-Synuclein (D37A6) XP® Rabbit mAb #4179 – W, IP, IHC-P, **IF-F**



Phospho-Tau (Thr205) (E7D3E) Rabbit mAb #49561: IHC analysis of paraffin-embedded human Alzheimer's disease brain using #49561 in the presence of non-phospho-Tau (Thr205) peptide (left) or phospho-Tau (Thr205) peptide (right).



β-Amyloid (D54D2) XP® Rabbit mAb #8243: Confocal IF analysis of paraffin-embedded human Alzheimer's brain using #8243 (green) and Tau (Tau46) Mouse mAb #4019 (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



α-Synuclein (D37A6) XP® Rabbit mAb #4179: Confocal IF analysis of normal rat cerebellum, hippocampus, and striatum using #4179 (green). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).

DRIVERS OF NEURODEGENERATION:

Neuroinflammation

Neuroinflammation is a condition observed in the CNS in response to infection, toxic metabolites, traumatic injury, or autoimmunity. Immune cells, such as microglia, macrophages, and neuroepithelium-derived astrocytes, monitor synaptic homeostasis and facilitate the clearance of apoptotic cells in response to injury in the CNS to protect brain function. The immune system may play a significant role in shaping the brain during development and mediating damage, regeneration, and repair. These processes may be compromised in neurodegenerative diseases. Interested in better understanding neuroinflammation?

Start with These Targets

TREM2

TREM2 is an immune receptor expressed on the cell surface of microglia, macrophages, osteoclasts, and immature dendritic cells. TREM2 forms a receptor-signaling complex with DAP12 to initiate cellular events like phagocytosis. TREM2 signaling is critical for the activation of microglia and may contribute to Alzheimer's disease pathogenesis by impairing microglia response, which leads to a buildup of β-amyloid.

TREM2 (D8I4C) Rabbit mAb #91068 – W, IP, **IF-IC**, IF-F

CD11b/ITGAM

Cluster of differentiation molecule 11b (CD11b)/Integrin alpha M (ITGAM) is a transmembrane protein forming heterodimers that are composed of α and β subunits. CD11b/ITGAM is expressed by, and commonly used as a marker for, myeloid lineage cells such as neutrophils, monocytes, macrophages, and microglia.

CD11b/ITGAM (M1/70) Rat mAb #46512 – IF-F

CD11c/ITGAX

CD11c/ITGAX is a dendritic cell marker that forms a heterodimer with CD18. Transcriptional profiling of the brains from beta-amyloid mouse models revealed a TREM2-dependent increase in CD11c/ITGAX expression in microglia. Therefore, CD11c/ITGAX may serve as a marker of microglia associated with stage 2 disease. Changes in CD11c/ITGAX expression have also been observed in Huntington's disease and amyotrophic lateral sclerosis.

CD11c (D1V9Y) Rabbit mAb #97585 – W, IHC-P, IF-IC, IF-F

iNOS

Inducible nitric oxide synthase (iNOS) expression has been observed in brain glial cells and invading macrophages in response to injury. It is normally induced in an oxidative environment or in response to proinflammatory cytokines. iNOS has been linked with Alzheimer's disease and Parkinson's disease.

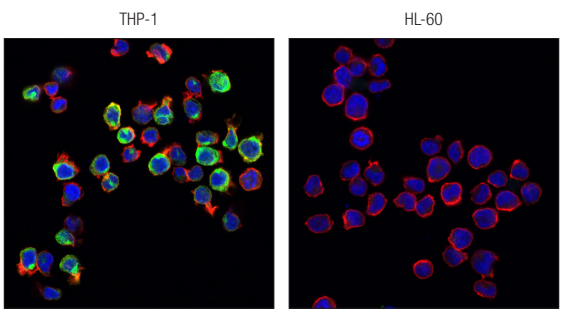
iNOS (D6B6S) Rabbit mAb #13120 – W, IP, IF-IC, F

Iba1/AIF-1

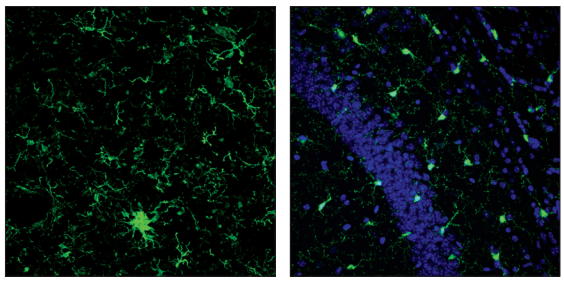
Iba1/AIF-1 is uniquely expressed in cells of monocytic lineage and is, therefore, widely used as a marker for microglia/macrophages in the brain and other tissue. Iba1/AIF-1 was originally cloned from activated macrophages in human atherosclerotic allogenic heart grafts undergoing chronic transplant rejection as well as from rat monocytes. Its function is not very well understood, but, as an F-actin-binding protein, Iba1/AIF-1 may function to remodel the actin cytoskeleton of microglia/macrophages.

Iba1/AIF-1 (E4O4W) XP® Rabbit mAb #17198 – W, IP, IHC-P, IF-IC, **IF-F**, F

Iba1/AIF-1 (E5N4J) Mouse mAb (IHC Formulated) #58970 – IHC-P



TREM2 (D8I4C) Rabbit mAb #91068: Confocal IF analysis of THP-1 (positive, left) and HL-60 (negative, right) cells using #91068 (green). Actin filaments were labeled with DyLight™ 554 Phalloidin #13054 (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



Iba1/AIF-1 (E404W) XP® Rabbit mAb #17198: Confocal IF analysis of human cortex (left) and mouse CA1 hippocampus (right) using I#17198 (green). In mouse tissue sections, cell nuclei were labeled with DAPI (blue). Images kindly provided by Dr. Simone Brioschi and Dr. Marco Colonna (Washington University) and used with permission.

DRIVERS OF NEURODEGENERATION:

Altered Cell Signaling

Abnormal cell-cell communication, for example disrupted presynaptic input, as well as disrupted intracellular signaling contribute to the pathogenesis of neurodegenerative disease. Understanding the signal transduction pathways that regulate gene expression will help understand disease initiation and progression, thereby informing efforts to develop therapeutic interventions. Interested in better understanding altered cell signaling?

Start with These Targets

CREB

CREB signaling is a cellular transcription factor that plays an important role in the formation of memories. Perturbed signaling has been observed in the brains of Alzheimer's disease mouse models, suggesting CREB signaling may be disrupted in human Alzheimer's disease brains as well. Disturbances in CREB function may also contribute to the development and progression of Huntington's disease.

CREB (48H2) Rabbit mAb #9197 – W, IP, IHC-P, IHC-F, IF-F, **IF-IC,** ChIP, ChIP-seq, F

Phospho-CREB (Ser133)

CREB is a cellular transcription factor activated when phosphorylated on Ser133. pCREB (Ser133) levels are reduced in the prefrontal cortex of patients with Alzheimer's disease, indicating a dysfunction in CREB signaling. Reduced pCREB levels in the peripheral blood mononuclear cells (PBMCs) of patients with Alzheimer's disease correlate with pCREB levels observed in postmortem Alzheimer's disease brains, suggesting pCREB expression in PBMCs may be a potential biomarker for disease progression.

Phospho-CREB (Ser133) (87G3) Rabbit mAb #9198 – W, IHC-P, **IF-IC,** IF-F, ChIP, ChIP-seq, F

GSK-3β

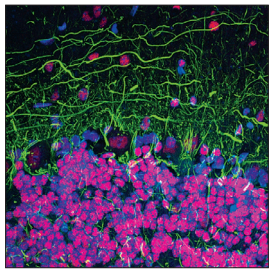
GSK-3β is known to interact with Tau, beta-amyloid, and α-synuclein and is implicated in the pathogenesis of Alzheimer's disease and Parkinson's disease. It is one of the kinases responsible for Tau hyperphosphorylation, resulting in neurofibrillary tangles. GSK-3β regulates several critical cellular events, such as axonal transport, microtubule dynamics, apoptosis, and inflammation, making GSK-3β a potential therapeutic target.

GSK-3β (D5C5Z) XP® Rabbit mAb #12456 – W, IP, **IHC-P**, IF-IC, F

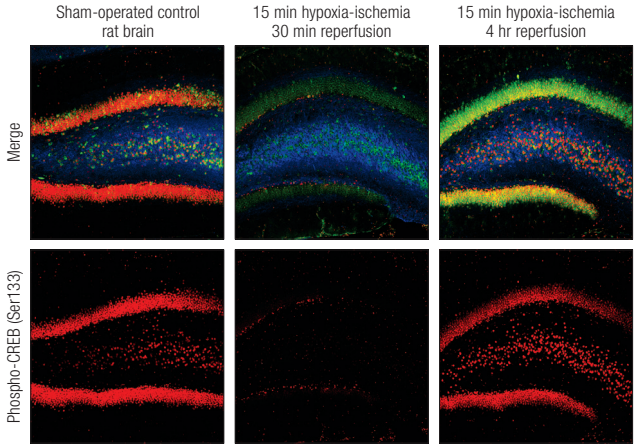
Phospho-GSK-3β (Ser9)

Phosphorylation of GSK-3β on Ser9 inactivates the protein, influencing its ability to regulate glycogen synthesis in response to insulin. In Alzheimer's disease mouse models, GSK-3β Ser9 phosphorylation may also reduce APP processing by β-secretase, decreasing Aβ production..

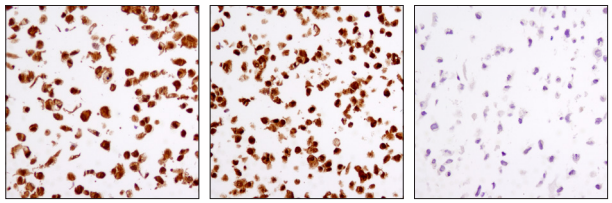
Phospho-GSK-3β (Ser9) (D85E12) XP® Rabbit mAb #5558 – W, IP, IF-IC, F



CREB (48H2) Rabbit mAb #9197: Confocal IF analysis of mouse cerebellum using #9197 (red) and Neurofilament-L (DA2) Mouse mAb #2835 (green). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



Phospho-CREB (Ser133) (87G3) Rabbit mAb #9198: Confocal IF images of dentate gyrus labeled with #9198 (red), Neurofilament-L (DA2) Mouse mAb #2835 (blue) and Phospho-S6 Ribosomal Protein (Ser235/236) (2F9) Rabbit mAb (Alexa Fluor® 488 Conjugate) #4854. Sections were obtained from a sham-operated control rat (left) or rats subjected to 15 min of hypoxia-ischemia followed by 30 min (left) or 4 h reperfusion (right).



GSK-3β (D5C5Z) XP® Rabbit mAb #12456: IHC analysis of paraffin-embedded MEF cell pellets, wild type (left), GSK-3α (-/-) (middle) and GSK-3β (-/-) (right) using #12456. (MEF wild type, GSK-3β (-/-), and GSK-3α (-/-) cells were kindly provided by Dr. Jim Woodgett, University of Toronto, Canada.)

DRIVERS OF NEURODEGENERATION:

Altered Epigenetics

Epigenetic regulation, including aberrant DNA methylation and histone modifications, have been linked to Alzheimer's disease, Huntington's disease, Parkinson's disease, multiple sclerosis, and amyotrophic lateral sclerosis. However, the exact effects on disease progression are unclear. Brain health is heavily reliant on epigenetic mechanisms, and loss of chromatin dynamics is observed in neurodegenerative diseases. Modifying the environment and targeting sites of potential risk for epigenetic changes are growing areas in the development of therapies against neurodegeneration. Interested in better understanding altered epigenetics?

Start with These Targets

5-hmC

5-hydroxymethylcytosine (5-hmC) is a novel modified cytosine oxidized from 5-mC (5-methylcytosine) by the Tet protein family. The pattern of 5-hmC throughout development is essential for proper neurodevelopment and neurological function. Dysregulation leads to neurodegenerative diseases like Alzheimer's disease and Huntington's disease; however, the exact mechanism of action remains to be determined.

5-Hydroxymethylcytosin (5-hmC) (HMC31) Mouse mAb #51660 – Dot blot, MeDIP, IF-IC

5-mC

5-methylcytosine (5-mC) is the most common state of cytosine in the brain after the unmodified state. As cells age, total genomic 5-mC content decreases in the brain. Decreased global 5-mC has been observed in Alzheimer's disease neurons and dysregulation of 5-mC may contribute to progression of amyotrophic lateral sclerosis and Parkinson's disease.

5-Methylcytosine (5-mC) (D3S2Z) Rabbit mAb #28692 – Dot blot, MeDIP, IF-IC

HDAC2

HDAC2 is a class I histone deacetylase that typically leads to gene repression. Deletion of HDAC2 in mouse Alzheimer's disease models results in improved cognition and decreased amyloid load. Increased HDAC2 expression has also been observed in Alzheimer's disease patients. HDAC2 is implicated in Huntington's disease and multiple sclerosis as well.

HDAC2 (D6S5P) Rabbit mAb #57156 – W, IP, ChIP, **ChIP-seq,** IF-IC

HDAC6

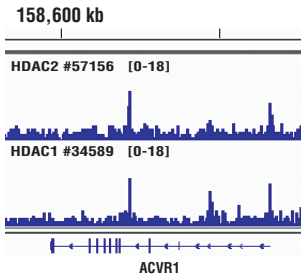
HDAC6 is a class II histone deacetylase with increased expression in the cortex and hippocampus of patients with Alzheimer's disease. HDAC6 colocalizes with Tau proteins and correlates with Tau phosphorylation. Decreasing HDAC6 levels may result in improved cognition.

HDAC6 (D2E5) Rabbit mAb #7558 – W, IP, IHC-P, **IF-IC**, F

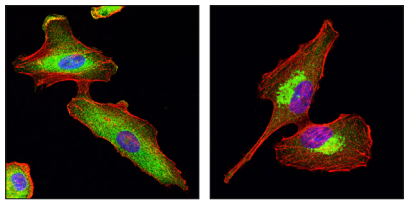
p300

p300 is a histone acetyltransferase that plays a role in the chromatin acetylation that is modulated in response to neuronal activity. Neuronal histone acetylation levels are lower in Alzheimer's disease mouse models, and activation of amyloid precursor protein-dependent signaling results in reduced histone acetyltransferase levels in primary neuronal cultures. p300 also plays a role in Huntington's disease and Parkinson's disease.

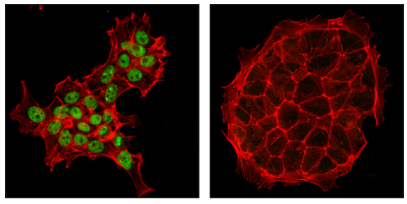
p300 (D8Z4E) Rabbit mAb #86377 – W, IP, IHC-P, **IF-IC**



HDAC2 (D6S5P) Rabbit mAb #57156: Chromatin immunoprecipitations were performed with cross-linked chromatin from K-562 cells and either #57156 or HDAC1 (D5C6U) XP® Rabbit mAb #34589, using SimpleChIP® Plus Enzymatic Chromatin IP Kit (Magnetic Beads) #9005. DNA libraries were prepared using SimpleChIP® ChIP-seq DNA Library Prep Kit for Illumina® #56795. HDAC2 and HDAC1 are known to have a similar binding pattern on chromatin. The figure shows binding of both HDAC2 and HDAC1 across ACVR1 gene. For additional ChIP-seq tracks, please download the product data sheet.



HDAC6 (D2E5) Rabbit mAb #7558: Confocal IF analysis of A549 cells, untreated (left) or treated with MG132 (5 µM, 24 hr; right), using #7558 (green). Actin filaments were labeled with DY-554 phalloidin (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



p300 (D8Z4E) Rabbit mAb #86377: Confocal IF analysis of 293T cells (left, positive) and HCT-15 cells (right, negative) using #86377 (green). Actin filaments were labeled with DyLight™ 554 Phalloidin #13054 (red).

DRIVERS OF NEURODEGENERATION:

Altered Metabolism

The three main purposes of metabolism are the conversion of food to energy; the conversion of nutrients to proteins, carbohydrates, lipids, and nucleic acids; and the elimination of nitrogenous wastes. There is a strong correlation between metabolic changes and/or dysfunction with neurodegenerative diseases. In particular, abnormal glucose tolerance or insulin resistance are observed in many neurodegenerative conditions. It is not clear whether metabolic changes are a cause or a consequence; however, understanding the role altered metabolism plays in disease progression is important, since these changes are associated with all neurodegenerative diseases. Interested in better understanding altered metabolism?

Start with These Targets

Phospho-AKT (Ser473)

AKT is a critical player in cellular processes, such as glucose metabolism, cell survival, cell growth, and migration. AKT is activated when phosphorylated on Ser473 in response to insulin to regulate glucose transport. AKT is associated with Alzheimer's disease; however, its actual role is not well understood. Its importance is recognized as it promotes Tau hyperphosphorylation. AKT is also implicated in Parkinson's disease.

Phospho-Akt (Ser473) (D9E) XP® Rabbit mAb #4060 – W, IP, IHC-P, **IF-IC**, F

Phospho-mTOR (Ser2448)

The mammalian target of rapamycin (mTOR) functions as an ATP and amino acid sensor that balances nutrient availability and cell growth. It is a part of the insulin and PI3K signaling pathway and is a core component of mTORC complexes. mTOR is implicated in neurogenerative diseases such as Huntington's disease and Alzheimer's disease.

Phospho-mTOR (Ser2448) (D9C2) XP® Rabbit mAb #5536 – W, IP, **IF-IC**

Phospho-AMPKα (Thr172)

AMPKα is a central regulator of metabolism and is phosphorylated in response to low ATP levels. Activated AMPKα initiates downstream events to influence glucose and lipid metabolism. AMPKα dysregulation is associated with Alzheimer's disease and amyotrophic lateral sclerosis.

Phospho-AMPKα (Thr172) (D4D6D) Rabbit mAb #50081 – W, IP, **IHC-P**

Phospho-S6 Ribosomal Protein (Ser235/236)

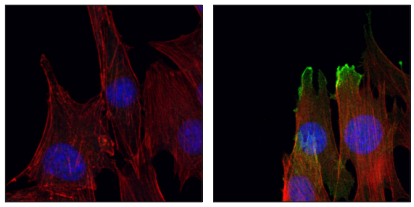
S6 ribosomal protein is commonly used as a marker for neuronal activity and a readout for mTORC1 activity. Phosphorylation of this ribosomal protein is altered in Huntington's disease and Alzheimer's disease.

Phospho-S6 Ribosomal Protein (Ser235/236) (E2R10) Mouse mAb #62016 – W, IF-IC

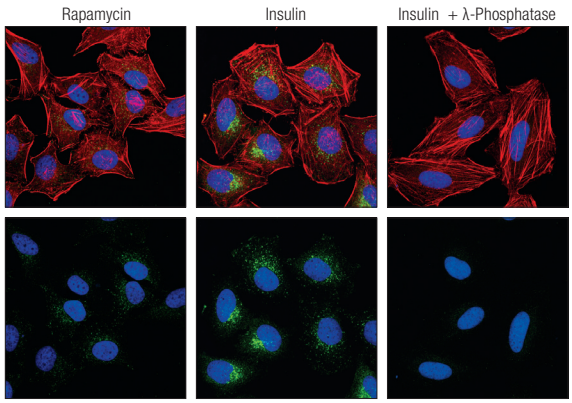
ApoE4

Apolipoproteins are transporters of lipids and cholesterol. ApoE4 is produced in the liver and brain and is linked to neuronal plasticity and synaptogenesis. People who carry the APOE4 allele are at higher risk of developing Alzheimer's disease, though the exact function of ApoE4 in Alzheimer's disease etiology remains unknown. The presence of the APOE4 allele also correlates with earlier onset of Parkinson's disease.

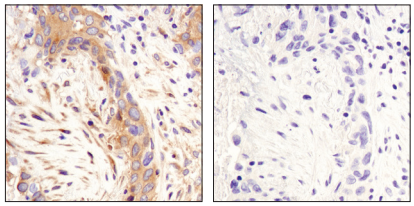
ApoE4 (4E4) Mouse mAb #8941 - W



Phospho-Akt (Ser473) (D9E) XP® Rabbit mAb #4060: Confocal IF analysis of C2C12 cells, LY294002-treated (left) or insulin-treated (right), using #4060 (green). Actin filaments have been labeled with Alexa Fluor® 555 Phalloidin #8953 (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



Phospho-mTOR (Ser2448) (D9C2) XP® Rabbit mAb #5536: Confocal IF analysis of HeLa cells, rapamycin-treated (#9904, 10 nM, 2 hr, left), insulin-treated (50 nM, 6 min, middle) or insulin- and λ-phosphatase-treated (right), using #5536 (green). Actin filaments were labeled with DY-554 phalloidin. Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



Phospho-AMPKα (Thr172) (D4D6D) Rabbit mAb #50081: IHC analysis of paraffin-embedded human lung carcinoma using #50081 in the presence of control peptide (left) or antigen-specific peptide (right).

DRIVERS OF NEURODEGENERATION:

Acquiring Cell Death

Mutations in cell death pathways, such as apoptosis, mitophagy, necroptosis, and autophagy, contribute to neuronal cell death and the progression of neurodegenerative diseases. Aberrant pro- and anti-apoptotic signaling, mitochondrial dysfunction, misregulation of autophagy or the unfolded protein response, and activation of the necrosome by stress and/or inflammation highlight just a few of the mechanisms by which neurons die or become diseased. Although many of these pathways are understood in non-neuronal cells, their mechanism of activation and dysregulation remains a mystery in neurons which present their own challenges. Interested in better understanding acquiring cell death?

Start with These Targets

Cleaved PARP (ASP214)

PARP typically functions as a key player in the DNA repair pathway in response to oxidative stress. When cleaved by caspase 3 between Asp214 and Gly215, the N-terminal cleaved fragment inhibits DNA repair enzymes to push neurons toward apoptosis, making it a hallmark of apoptotic cells.

Cleaved PARP (Asp214) (D64E10) XP® Rabbit mAb #5625 – W, IP, IHC-P, IF-IC, F

PINK1

PINK1 typically functions as a key player in the DNA repair pathway in response to oxidative stress. When cleaved by caspase 3 between Asp214 and Gly215, the N-terminal cleaved fragment inhibits DNA repair enzymes to push neurons toward apoptosis, making it a hallmark of apoptotic cells.

PINK1 (D8G3) Rabbit mAb #6946 – W, IP

SQSTM1/p62

Sequestosome 1 (SQSTM1/p62) is an autophagosome cargo protein that binds to protein aggregates to target them for selective autophagy. SQSTM1/p62 mutations lead to an increase in intracellular aggregation of α-synuclein, Huntingtin, Tau protein, and beta-amyloid to drive progression of Parkinson's disease, Huntington's disease, and Alzheimer's disease, respectively.

SQSTM1/p62 (D10E10) Rabbit mAb (IF Preferred) #7695 – IP, IF-IC

LC3A/B

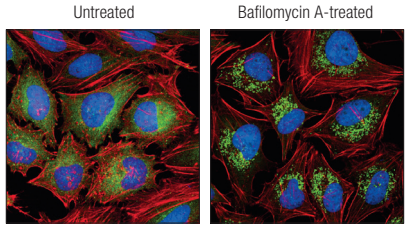
LC3A/B plays a critical role in autophagosome biogenesis and maturation and also functions as an adaptor protein to selectively recruit cargo to the autophagosome. An increase in LC3-positive microglia have been observed in tissues in Alzheimer's disease patients with TREM2 mutations, suggesting that disruptions in TREM2-dependent autophagy can contribute to Alzheimer's disease etiology.

LC3A/B (D3U4C) XP® Rabbit mAb #12741 – W, IHC-P, IF-IC, F

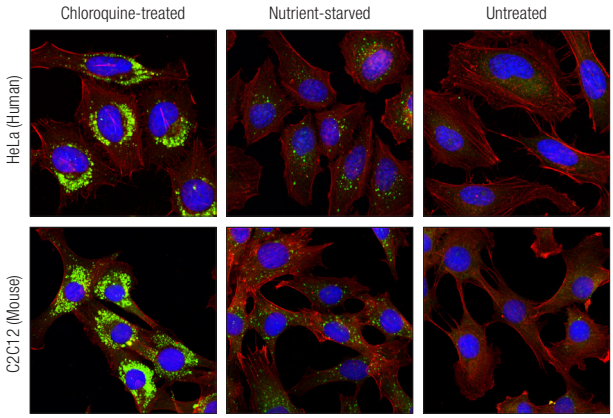
Phospho-RIP3 (Ser227)

Human Phospho-RIP3 (Ser227) phosphorylates MLKL1 to trigger TNF-induced necroptosis. This form of programmed cell death has been reported in multiple sclerosis and amyotrophic lateral sclerosis.

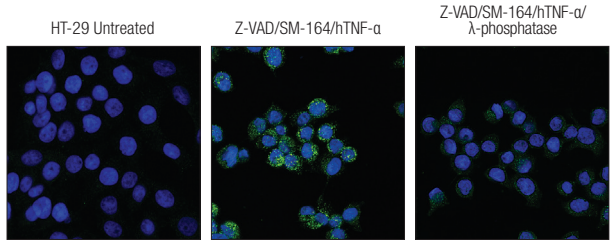
Phospho-RIP3 (Ser227) (D6W2T) Rabbit mAb #93654 – W, IF-IC



SQSTM1/p62 (D10E10) Rabbit mAb (IF Preferred) #7695: Confocal IF analysis of HeLa cells, untreated (left) or treated with bafilomycin A (100 nM, 18 hr; right), using #7695 (green). Actin filaments were labeled with DY-554 phalloidin. Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



LC3A/B (D3U4C) XP® Rabbit mAb #12741: Confocal IF analysis of HeLa (upper) and C2C12 (lower) cells, chloroquine-treated (50 µM, overnight; left), nutrient-starved with EBSS (3 hr, middle) or untreated (right) using #12741 (green) and β-Actin (13E5) Rabbit mAb (Alexa Fluor® 555 Conjugate) #8046 (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).



Phospho-RIP3 (Ser227) (D6W2T) Rabbit mAb #93654: Confocal IF analysis of HT-29 cells, untreated (A), pretreated with Z-VAD (20 µM, 30 min) followed by treatment with SM-164 (100 nM) and Human Tumor Necrosis Factor-α (hTNF-α) #8902 (20 ng/mL, 6 hr; B), or pretreated with Z-VAD followed by treatment with SM-164 and hTNF-α and post-processed with λ-phosphatase (C), using #93654 (green). Actin filaments were labeled with DyLight™ 554 Phalloidin #13054 (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).

DRIVERS OF NEURODEGENERATION:

Acquiring Senescence

Cellular senescence is characterized by irreversible cell-cycle arrest in combination with a distinct secretory phenotype and expanded lysosomes in response to stress. Senescent cells accumulate in tissues during aging, and various markers of senescence are associated with neurodegenerative disease. p16 accumulates in senescent astrocytes and microglia in the context of Tau pathology. p16 and p27 accumulate in senescent oligodendrocyte progenitor cells (OPCs) in the context of amyloid plaque pathology. Senolytic compounds are investigated to remove senescent cells and treat Alzheimer's disease. Interested in better understanding acquiring senescence?

Start with These Targets

p16 INK4A

p16 is a member of the INK4 family of cyclin-dependent kinase inhibitors that are responsible for arresting the cell cycle in the G1 phase. p16 is commonly used as a marker for senescent cells. Elevated expression of p16 has been observed in the neurons of Alzheimer's disease patients and may also play a role in the progression of multiple sclerosis.

p16 INK4A (D7C1M) Rabbit mAb #80772 – W, IP, F

p21 Waf1/Cip1

p21 Waf1/Cip1, a CDK inhibitor, is a common marker of cellular senescence. It causes cell cycle arrest in response to stress-induced p53 to trigger senescence. p21 may be a critical mediator of cell cycle dysregulation in Alzheimer's disease.

p21 Waf1/Cip1 (12D1) Rabbit mAb #2947 – W, IP, IHC-P, **IF-IC**, F

IL-1β

IL-1β is a pro-inflammatory cytokine that is secreted by senescent cells. It is elevated in Alzheimer's disease brain tissue, cerebral spinal fluid (CSF), and serum, potentially due to increased p38MAPK activity. Aged in vitro rat microglia may acquire a senescent phenotype characterized by increased levels of IL-1β and TNF-α after treatment with beta-amyloid oligomers. Elevated levels of IL-1β have also been observed in the CSF, serum, and dopaminergic regions of the striatum from patients with Parkinson's disease.

IL-1β (D3U3E) Rabbit mAb #12703 – W, IF-IC, **F**

TNF-α

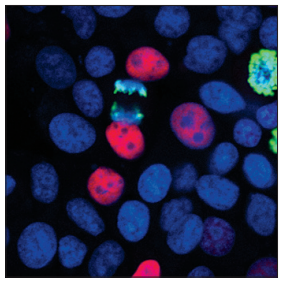
TNF-α is a cytokine whose dysregulation has been implicated in Alzheimer's disease and Parkinson's disease. Levels of TNF-α are increased in the brain tissue, CSF, and serum of Alzheimer's disease patients, potentially due to increased p38MAPK activity. Aged in vitro rat microglia may acquire a senescent phenotype characterized by increased levels of IL-1β and TNF-α after treatment with beta-amyloid oligomers. Elevated levels of TNF-α have also been observed in the CSF, serum, and dopaminergic regions of the striatum from patients with Parkinson's disease.

TNF-α (D2D4) XP® Rabbit mAb (Mouse Specific) #11948 – W, IP, **IF-IC**, F

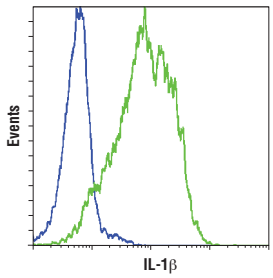
β-Galactosidase

Senescent cells can be identified by an increased level of lysosomal β-galactosidase activity. Beta-amyloid triggers senescence in in vitro models, driving expression of p16 INK4A and senescence-associated β-galactosidase. Increased β-galactosidase activity has also been observed in the CSF of Parkinson's disease patients.

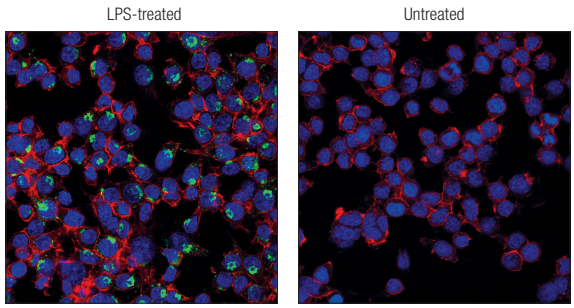
Senescence β-Galactosidase Staining Kit #9860



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).



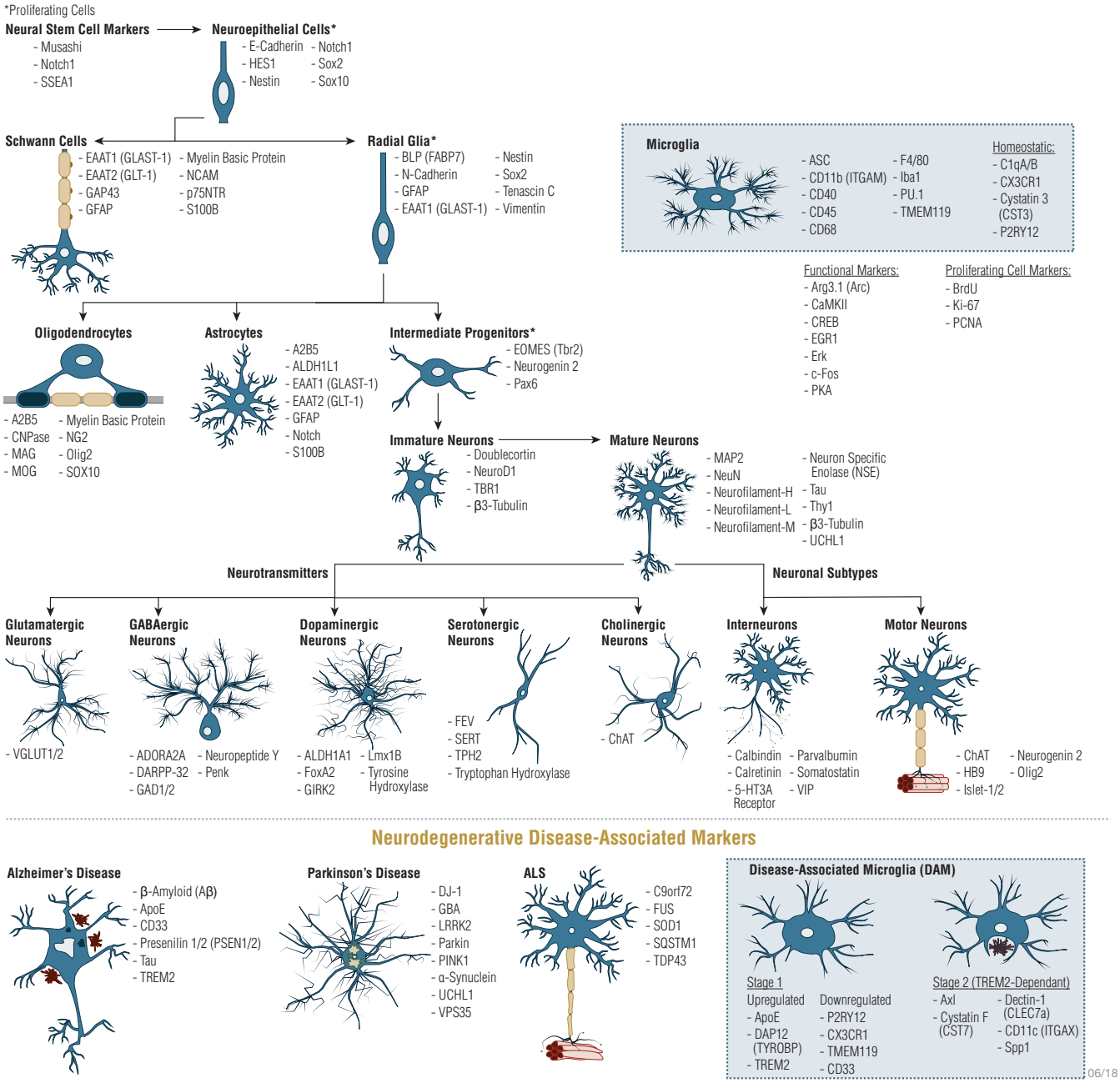
IL-1β (D3U3E) Rabbit mAb #12703: Flow cytometric analysis of THP-1 cells, untreated (blue) or LPS-treated (100 ng/ml, 3 hr; green), using #12703. Anti-rabbit IgG (H+L), $F(ab')_2$ Fragment (Alexa Fluor® 647 Conjugate) #4414 was used as a secondary antibody.



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 (Rodent Specific) (green). Actin filaments were labeled with DY-554 phalloidin (red). Blue pseudocolor = DRAQ5® #4084 (fluorescent DNA dye).

Neuronal and Glial Cell Marker Atlas

Cell Type Markers



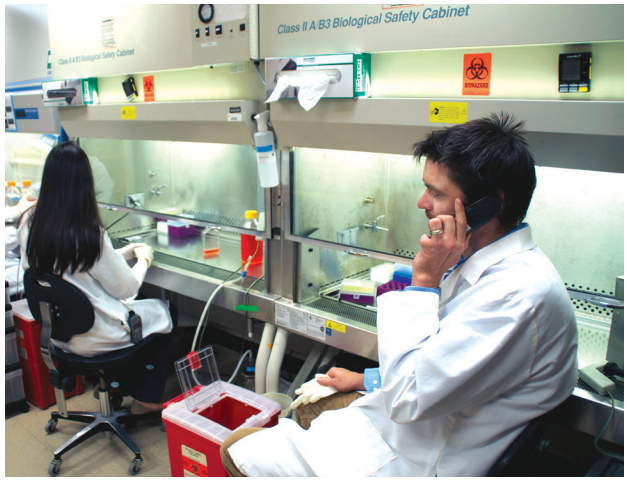
Neurodegenerative Disease-Associated Markers

06/18

Technical Support

At CST, providing exceptional customer service and technical support are top priorities. Our scientists work at the bench daily to produce and validate our antibodies, so they have hands-on experience and in-depth knowledge of each antibody's performance. In the process, these same scientists generate valuable reference information that they use to answer your questions and help troubleshoot your experiment by phone or email.

For questions about how to customize your protocol, please contact technical support by emailing support@cellsignal.com, visiting **www.cellsignal.com/support**, or calling 1-877-678-8324.



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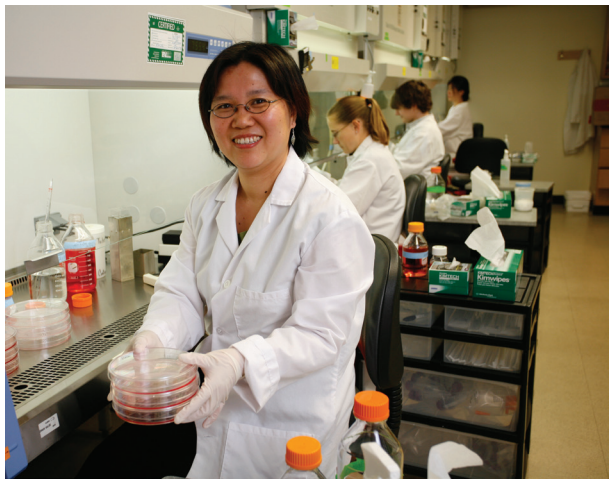

Founded by research scientists in 1999, Cell Signaling Technology (CST) is a private, family-owned company with over 400 employees worldwide. Active in the field of applied systems biology research, particularly as it relates to cancer, CST understands the importance of using antibodies with high levels of specificity and lot-to-lot consistency. That's why we produce all of our antibodies in house and perform painstaking validations for multiple applications. And the same CST scientists who produce our antibodies also provide technical support for customers, helping them design experiments, troubleshoot, and achieve reliable results.

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PR944_Hallmarks of Neurodegeneration_0922

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