DRIVERS OF NEURODEGENERATION: Acquiring Cell Death

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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

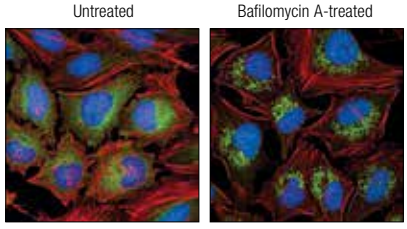
LC3A/B plays a critical role in autophagosome biogenesis and maturation and also functions as an adaptor protein to selectively recruit cargo to the autophagosome. An increase in LC3-positive microglia have been observed in tissues in Alzheimer's disease patients with TREM2 mutations, suggesting that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

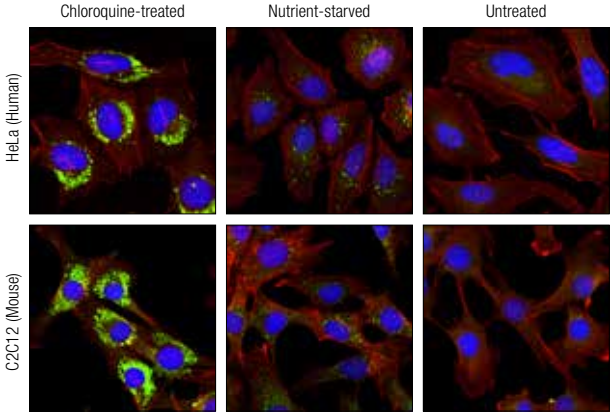
Phospho-RIP3 (Ser227)

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.

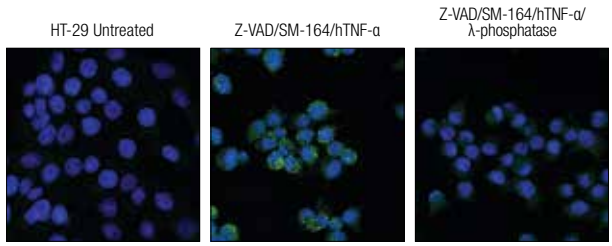
Phospho-RIP3 (Ser227) (D6W2T) Rabbit mAb #93654 – W, IF-IC



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 (IF preferred) (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).

Learn more about the Hallmarks of Neurodegeneration at:
cst-science.com/ndg-hallmarks

Cell Signaling TECHNOLOGY®

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