

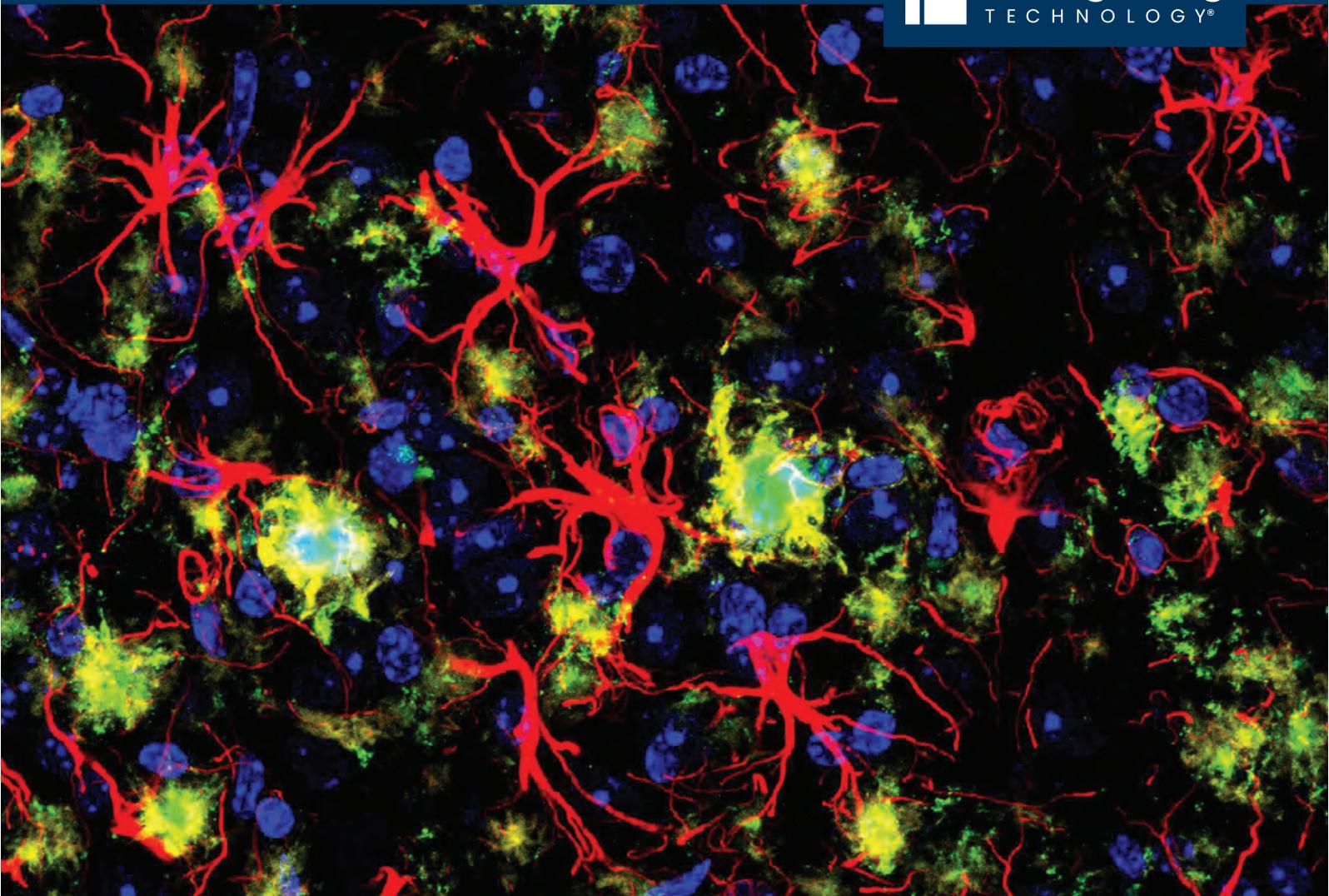
SOLUTIONS FOR

# Advancing Neurodegeneration Therapeutics Discovery

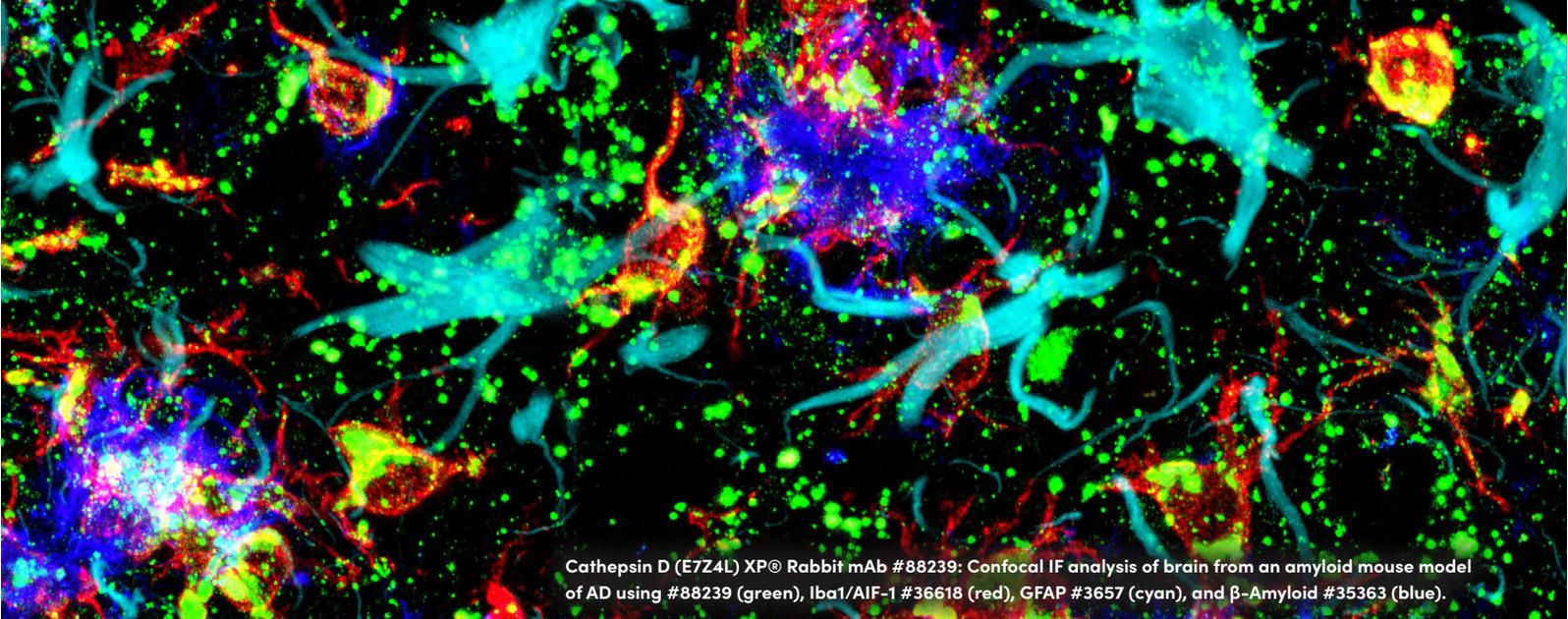
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**Cell Signaling**  
TECHNOLOGY<sup>®</sup>



**β-Amyloid (1-43) (E8C2D) Rabbit mAb #32098:** Confocal IF analysis of brain from an amyloid mouse model of Alzheimer's disease using #32098 (green), GFAP #3656 (red), β-Amyloid #42284 (yellow), and DAPI #8961 (blue).



Cathepsin D (E7Z4L) XP® Rabbit mAb #88239: Confocal IF analysis of brain from an amyloid mouse model of AD using #88239 (green), Iba1/AIF-1 #36618 (red), GFAP #3657 (cyan), and  $\beta$ -Amyloid #35363 (blue).

# Solutions That Move Your Discovery Forward

Put our experience to work for you. Cell Signaling Technology (CST) scientists are biology, application, and therapeutic area domain experts and are here to streamline your discovery. We are passionate about science and keep up with all the latest neurodegenerative disease research, allowing us to offer a broad antibody portfolio against targets that could lead to new, more efficacious therapies. CST also offers an extensive post-translational modification-specific antibody portfolio as well as resources like PhosphoSitePlus® PTM Database ([www.phosphosite.org](http://www.phosphosite.org)).

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# Tailor CST® Products & Services to Fit Your Project Needs



## Quality & Reproducibility

Reproducibility in your experiments is not a matter of chance. It is a matter of science. CST products are developed, tested, and rigorously validated across multiple applications by tenured CST scientists who understand the underlying biology. Over 99.5% of CST recombinant monoclonal antibodies are manufactured in-house, providing complete control over our supply chain and providing lot-to-lot consistency for the lifetime of your project.



## Assay Support & Flexibility

Your assay is only as good as your antibody is specific. CST antibodies and ready-to-use ELISA and cellular assay kits are developed with this in mind. They are designed to seamlessly fit into your assay workflow and instantly answer key questions. CST subject matter experts are available to help identify the best readout and clone to effectively assess your therapeutic efficacy and safety.



## Companion Reagents

CST offers a wide selection of epitope-tagged and control antibodies, secondary antibodies, detection reagents, and experimental controls, as well as standard buffers and other reagents required to complete your experimental workflow.



## Services & Customization

Sometimes the fastest way to move your discovery forward is to have someone else prepare the tools you need. CST provides custom solutions that meet your specific research challenges, freeing up your time to focus on the science.

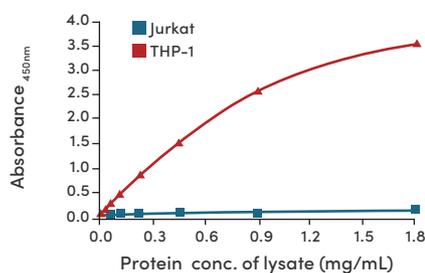
Services and Customized Offerings	Overview
<b>Carrier-Free and Customized Formulations</b>	Ideal for any application, assay, or platform requiring conjugation-ready or unique formulations, including multiplex IF and ELISA
<b>Custom Antibody Conjugation</b>	Have our in-house experts perform the conjugations you need for your assay: fluorophores, biotin, enzymes, select oligonucleotides, and more
<b>Proteomics Analytical Services</b>	Partner with CST for qualitative and quantitative protein profiling of your precious samples, including brain tissue. CST scientists are by your side from project planning to sample prep to data analysis, providing you with actionable results
<b>Bulk Quantities and Lot Reservation</b>	Eliminate potential supply problems by partnering with CST to reserve a single lot or place bulk orders
<b>Custom Peptides and Controls</b>	CST provides the controls you need for your specific assay

## Inflammation

Chronic neuroinflammation is associated with the progression of neurodegenerative diseases. Microglia are the resident macrophages of the central nervous system and have key roles in mediating neuronal signaling and neuroinflammatory responses. CST offers a wide variety of cell signaling markers associated with chronic neurodegenerative diseases that can be reliably utilized for determining disease onset and progression.

### TREM2 Signaling

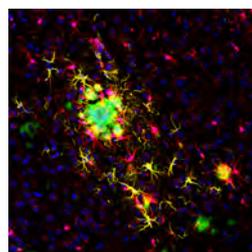
- TREM2 ELISA
- Syk/Phospho-Syk ELISA
- DAP12 (TYROBP)
- Pan Phospho-Tyrosine



FastScan™ Total TREM2 ELISA Kit #23831.

### Inflammasome

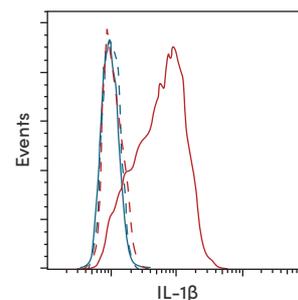
- ASC/TMS1
- Gasdermin D
- NLRP3
- IL-1 $\beta$ /Cleaved IL-1 $\beta$
- Caspase-1/Cleaved Caspase-1



**ASC/TMS1 (D2W8U) Rabbit mAb (Mouse Specific) (Alexa Fluor® 647 Conjugate) #23640:** Confocal IF analysis of mouse Tg2576 brain that overexpresses mutant human APP695 using #23640 (red), GFAP (Alexa Fluor® 555 Conjugate) #3656 (pseudocolor yellow),  $\beta$ -Amyloid (Alexa Fluor® 488 Conjugate) #51374 (green), and DAPI #4083 (blue).

### Cellular Readouts for Neuroinflammation

- IL-1 $\beta$ /6/10
- TNF- $\alpha$
- TGF- $\beta$
- Stat3
- Jak



**IL-1 $\beta$  (D3U3E) Rabbit mAb #12703:** Flow cytometric analysis of THP-1 cells untreated (blue) or treated (green) with LPS #14011 using #12703.

## Cell Death

Cell death serves as a readout for neurodegenerative disease progression. Neurons and glia can die and become diseased due to the aberrant regulation of cell death and survival pathways, which may include mitochondrial dysfunction, autophagy, and the activation of both apoptotic and non-apoptotic pathways. With validated antibodies, protocols, and sampler kits from Cell Signaling Technology (CST), neurodegenerative disease progression can be reliably assessed by analyzing the different types and activation states of cell death in human and rodent samples.

### Necroptosis

- RIP, Phospho-RIP (Ser166)/(Ser14)
- RIP3, Phospho-RIP3 (Ser227)/(Thr231/Ser232)
- MLKL, Phospho-MLKL (Ser358)/(Ser345)

### Apoptosis

- Caspase-3, Cleaved Caspase-3 (Asp175)
- PARP, Cleaved PARP (Asp214)
- Caspase-8, Cleaved Caspase-8 (Asp374)
- TUNEL Assay Kits

### Pyroptosis

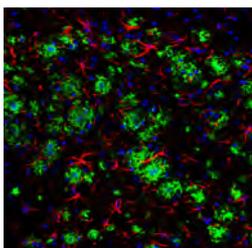
- Gasdermin D, Cleaved Gasdermin D (Asp275)/(Asp276)
- Cleaved IL-1 $\beta$  (Asp116)/(Asp117)
- Caspase-1, Cleaved Caspase-1 (Asp297)/(Asp296)

## Proteinopathies

The production and processing of proteins that form protein aggregates are associated with frontotemporal lobar degeneration and tauopathies. Therapies targeting protein aggregate formation may help slow proteinopathy progression. Protein aggregates found in blood or cerebrospinal fluid may also serve as biomarkers for diagnosing conditions earlier, and for monitoring disease progression and therapeutic response. Cell Signaling Technology® (CST®) antibodies are an ideal foundation for biomarker-based assays because they are thoroughly validated for specificity and sensitivity on biologically relevant binary model systems.

### ■ Amyloid

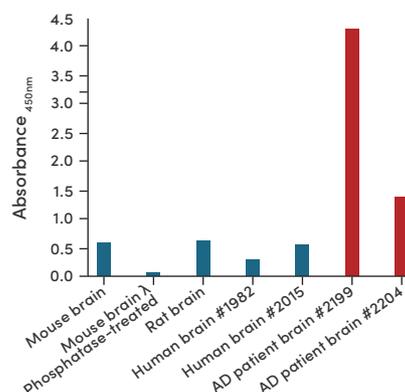
- APP
- $\beta$ -Amyloid
- $\beta$ -Amyloid (42/40)
- $\beta$ -Amyloid pyro E



**$\beta$ -Amyloid (D54D2) XP® Rabbit mAb #8243:** Confocal IF analysis of the subicular cortex from an amyloid mouse model of Alzheimer's disease mouse using #8243 (green), GFAP #3670 (red), and DAPI #8961 (blue).

### ■ Tau/Phospho-Tau

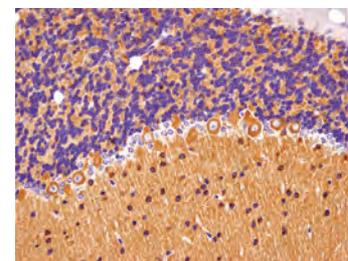
- ELISA Kits
- Antibody Sampler Kits
- Conjugates



**PathScan® Phospho-Tau (Thr217) Sandwich ELISA Kit #59672:** #59672 is sensitive enough to detect differences in Thr217 phosphorylation among different Alzheimer's disease patient samples, which may indicate disease progression.

### ■ Additional Neurodegenerative Aggregate Markers

- $\alpha$ -synuclein, Phospho- $\alpha$ -synuclein (Ser129)
- TDP43/FUS
- Huntingtin



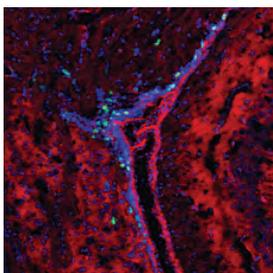
**Huntingtin (D7F7) XP® Rabbit mAb #5656:** IHC analysis of paraffin-embedded mouse cerebellum using #5656.

## Cell Viability

Measuring cell viability can serve as a readout for determining neuronal disease progression. Aberrant or reduced proliferation, increases in neural damage, and the accumulation of senescent cells are all indicators of cell health and neurodegenerative disease status. CST offers antibodies and assay kits to determine cell viability efficiently and economically.

### ■ Cell Proliferation Markers

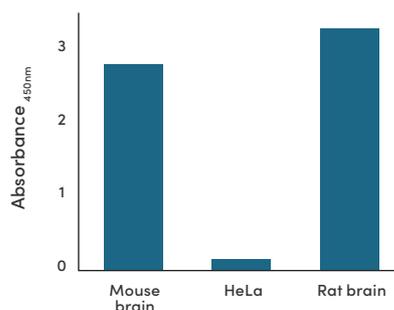
- BrdU ELISA & Flow Kits
- PCNA
- Ki-67



**Ki-67 (D3B5) Rabbit mAb #9129:** Confocal IF analysis of the ventricular zone in P21 mouse brain using #9129 (green). Actin filaments were labeled with DyLight™ 554 phalloidin #13054 (red) and DNA labeled with DRAQ5® #4084 (blue).

### ■ Neural Damage Markers

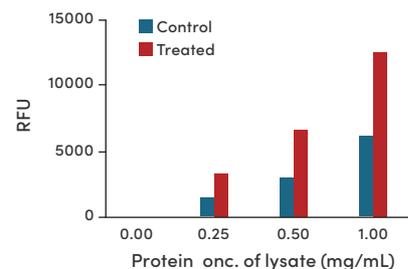
- Neurogranin
- Neurofilament-L



**PathScan® Total Neurofilament-L Sandwich ELISA Kit #99175:** Neurofilament-L protein is detectable in mouse and rat brain, but not HeLa cells (negative control) using #99175, as expected.

### ■ Senescence

- p16
- $\beta$ -galactosidase



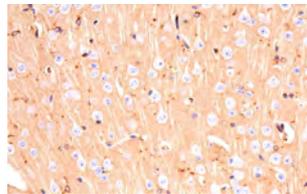
**Senescence  $\beta$ -Galactosidase Activity Assay Kit (Fluorescence, Plate-Based) #23833:**  $\beta$ -galactosidase activity in HeLa lysates untreated and treated with Doxorubicin using #23833.

# Metabolism

The human brain is responsible for about 20% of basal energy expenditure, despite accounting for only 2% of body weight. Metabolic dysregulation and neurodegeneration are strongly correlated. Metabolic proteins may act as therapeutic targets since abnormal glucose tolerance or insulin resistance is observed in many neurodegenerative conditions. Cell Signaling Technology (CST) provides high-quality antibodies and assays to support the interrogation of metabolic pathways and cellular energy homeostasis regulation.

## Metabolite Transporters

- ABCA1
- ABCA7
- ApoE4
- LRP1



**ApoE (E7X2A) Rabbit mAb #49285:**  
IHC analysis of paraffin-embedded mouse brain using #49285.

## Insulin Receptor Signaling

- Insulin receptor
- Akt
- CREB/Phospho-CREB
- Glycogen Synthase/Phospho-Glycogen Synthase
- GSK-3β/Phospho-GSK-3β
- PI3K
- PTEN
- PDK1

## Autophagy

- mTOR
- AMPK
- LC3B
- ULK1/Phospho-ULK1 (Ser757)/(Ser555)
- SQSTM1/p62
- TFEB/Phospho-TFEB (Ser211)

## Mitophagy

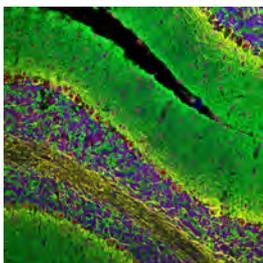
- Pink1
- Parkin/Phospho-Parkin (Ser65)
- DRP1
- Ubiquitin/Phospho-Ubiquitin (Ser65)
- TBK1/Phospho-TBK1 (Ser172)
- Optineurin/Phospho-Optineurin (Ser177)
- FUNDC1
- BNIP3/3L

# Synaptic Plasticity

Synaptic plasticity is not only a part of development, learning, and memory, but has also been utilized as a readout for the clinical diagnosis of neurodegenerative diseases, including synaptopathies like Alzheimer’s disease. CST provides high-quality antibodies and assays to support the interrogation of synaptic activity and function.

## Presynaptic Proteins

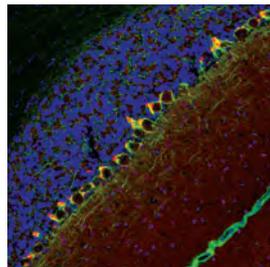
- Synaptophysin
- Synapsin-1/Phospho-Synapsin-1



**Synaptophysin (D8F6H) XP® Rabbit mAb #36406:** Confocal IF analysis of mouse brain using #36406 (green), Neurofilament-L #2835 (yellow), Lamin A/C (4C11) Mouse #4777 (red), and DAPI #8961 (blue).

## Postsynaptic Proteins

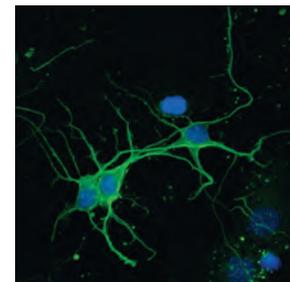
- PSD95/Phospho-PSD95
- AMPA Receptor 1 (GluA1)/Phospho-AMPA 1 (GluA1)
- NMDAR-1/Phospho-NMDAR-1



**PSD95 (D27E11) XP® Rabbit mAb #3450:** Confocal IF analysis of rat cerebellum using #3450 (red), Neurofilament-L #2835 (green), DRAQ5® #4084 (pseudocolor blue).

## Modulators of Synaptic Plasticity

- CaMKII
- Calcium Signaling
- CREB/Phospho-CREB



**CaMKII-α (6G9) Mouse mAb #50049:** Confocal IF analysis of primary neurons using CaMKII-α #50049 (green) and DRAQ5® #4084 (pseudocolor blue).

# Epigenetics

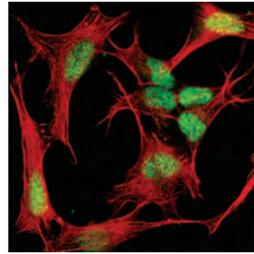
Brain health is heavily reliant on epigenetic mechanisms, and a loss of chromatin dynamics is observed in neurodegenerative diseases. Profiling epigenetic patterns and identifying the chromatin marks associated with disease progression have become increasingly important for the development of therapies against neurodegeneration. Cell Signaling Technology (CST) provides a comprehensive and diverse catalog of epigenetics products and an extensive assay portfolio used to measure protein-DNA interactions and histone modifications.

## Histone Modifications

- Acetyl-Histone H4 (Lys16)
- HDAC2/6
- p300
- SirT1
- REST, CoREST
- G9a/EHMT2
- LSD1

## DNA Methylation

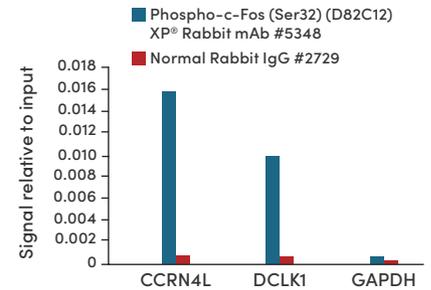
- 5-mC, 5-hmC
- DNMT1
- TET1
- MeCP2



**MeCP2 (D4F3) XP® Rabbit mAb #3456:**  
Confocal IF analysis of SH-SY5Y cells using #3456 (green) and actin (red).

## Immediate Early Genes and Associated Proteins

- CREB/Phospho-CREB
- c-Fos/Phospho-c-Fos
- EGR1



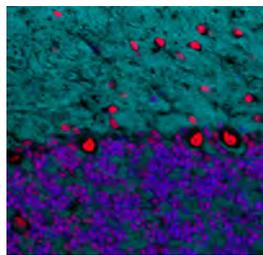
**Phospho-c-Fos (Ser32) (D82C12) XP® Rabbit mAb #5348:** qRT-PCR results for ChIP-enriched DNA from PC-12 cells starved overnight and treated with hβ-NGF #5221 and either #5348 or Normal Rabbit IgG #2729 using SimpleChIP® Enzymatic Chromatin IP Kit (Magnetic Beads) #9003

# RNA-Binding Proteins (RBPs)

RBPs are increasingly becoming therapeutic targets for the treatment of neurodegeneration. Dysregulation of RNA-binding proteins (RBPs) has been linked to amyotrophic lateral sclerosis (ALS), Alzheimer’s disease, and frontotemporal dementia. Mutations in stress granule-associated RBPs lead to the pathological accumulation of protein aggregates that are readily apparent in neurodegenerative disorders. Age-related changes in mRNA methylation and methylation-dependent RBPs have also been associated with neurodegeneration. CST offers antibodies against key RBPs, stress granules, and m6A methylators, validated in relevant neuronal systems.

## RBPs and Stress Granules

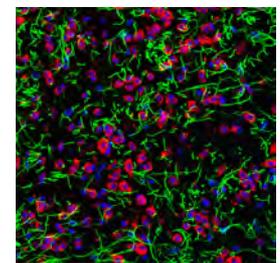
- TDP43, FUS
- TIA-1, TIAR
- FMRP
- G3BP1
- Ataxin-1/2



**TDP43 (D9R3L) Rabbit mAb (Alexa Fluor® 555 Conjugate) #68779:**  
Confocal IF analysis of mouse cerebellum using #68779 (red), Ras (Alexa Fluor® 647 Conjugate) #37182 (cyan pseudocolor), and DAPI #8961 (blue).

## RNA m6A Methylation

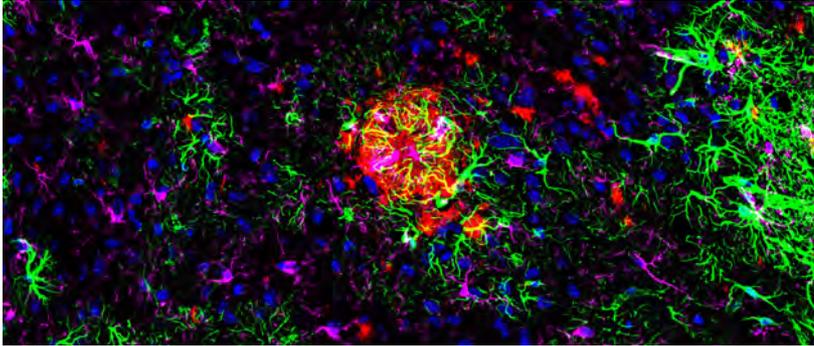
- N6-Methyladenosine
- METTL3/14
- FTO
- ALKBH5
- YTHDF1/2/3



**YTHDF2 (E212H) Rabbit mAb #71283:** Confocal IF analysis of mouse medulla oblongata using #71283 (red), GFAP (Alexa Fluor® 488 Conjugate) #3655 (green), and DAPI #8961 (blue).

## Multiplex Immunofluorescence (IF) Enablement

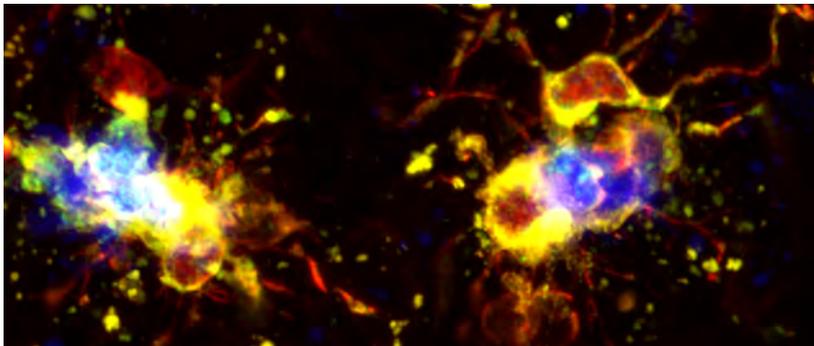
Cell Signaling Technology (CST) has the breadth of products available to enable several methods of multiplex staining, highlighted below.



Confocal IF analysis of mouse Tg2576 brain labeled with GFAP #34001 (green),  $\beta$ -Amyloid #15126 (red), HS1 #3892 (magenta), and DAPI #8961 (blue).

### ■ Host Species

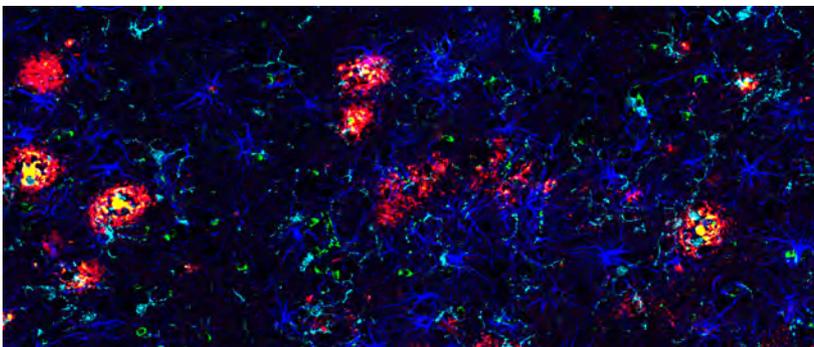
- One of the simplest ways to multiplex
- Use primary antibodies derived from various host species and isotypes (rabbit IgG, mouse IgG1, rat IgG2a, etc.), then probe with fluorophore-coupled secondaries specific to the host primary.



Confocal IF analysis of an amyloid mouse model of Alzheimer's disease brain using Alexa Fluor<sup>®</sup> 647 Conjugated Iba1/AIF-1 #78060 (red), Alexa Fluor<sup>®</sup> 488 Conjugated HS1 #68206 (green), GPNMB #90205 (yellow), and methoxy XO4 (blue). Image kindly provided by Dr. Simone Briochi of Dr. Marco Colonna's lab (Washington University) and used with permission.

### ■ Fluorophore Conjugated Antibodies

- Directly conjugate a primary antibody with a specific label, such as a fluorophore or enzyme
- CST offers rigorously validated, ready-to-use antibodies conjugated to the most popular fluorophores.



Multiplex IF imaging of the human prefrontal cortex from an Alzheimer's disease patient stained with GFAP (blue), microglia with Iba-1/AIF-1 #17198 (cyan), APOE #13366 (green), and  $\beta$ -Amyloid #9888 (red). Imaged with the Akoya PhenoCycler<sup>®</sup> platform. Image kindly provided by Akoya and used with permission.

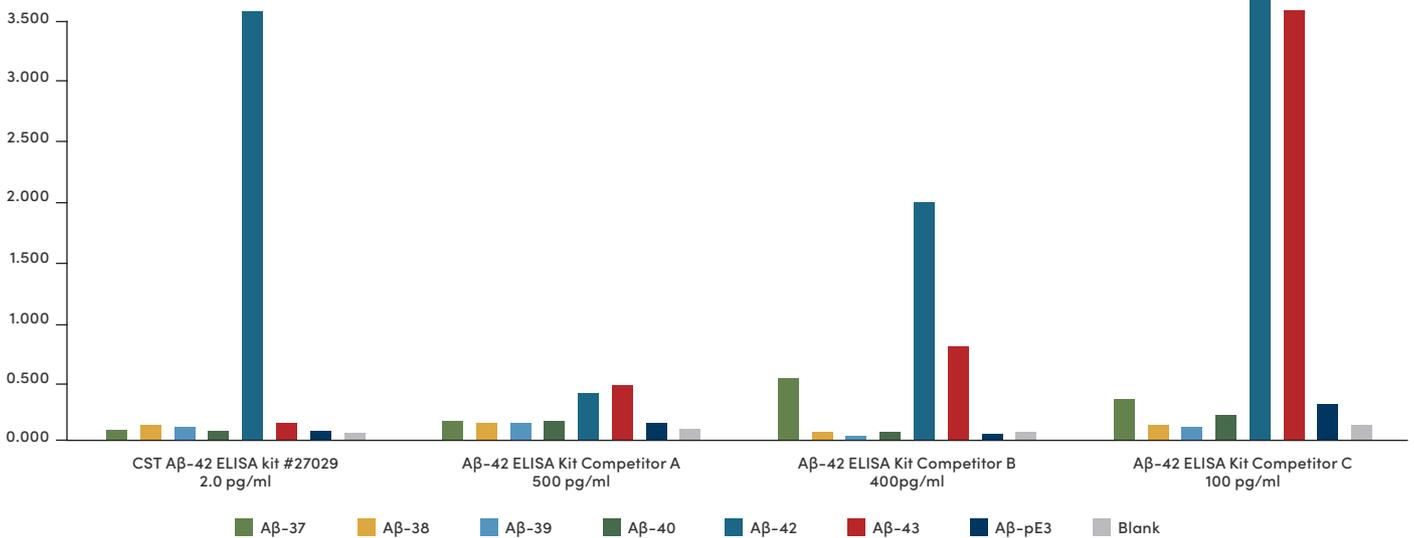
### ■ Conjugation-Ready Carrier-Free Antibodies

- Preferred method when expanding panels or using technologies where a directly conjugated antibody is not available.
- Use carrier-free formulated antibodies. They are conjugation-ready to support platforms requiring labels such as metals, fluorophores, and oligonucleotides.

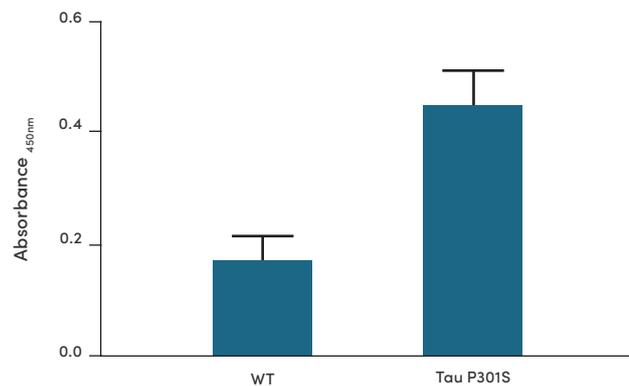
## Antibody Pairs for Platforms and ELISA

Rigorously validated antibody pairs are at the heart of every ELISA experiment. Cell Signaling Technology (CST) offers matched antibody pairs, both as a complete solution in sandwich ELISA kits or as custom pairs, ideal for incorporating into standard high-throughput ELISA-like assay platforms. These validated antibody pairs offer unrivaled specificity to deliver accurate readouts when monitoring therapeutic modulation of key neurodegenerative disease biomarkers. Some CST kits are sensitive to plasma proteins, enabling monitoring of disease status with live models.

## Measure Key Biomarkers with Highly Specific and Sensitive ELISA Kits



**The PathScan® β-Amyloid (1-42) Sandwich ELISA Kit #27029** is highly specific to only human Aβ-42, showing no significant signal with Aβ-37, Aβ-38, Aβ-39, Aβ-40, Aβ-43, or pE3 peptides, as expected. By contrast, other leading commercially available β-amyloid (1-42) sandwich ELISA kits show little-to-no specificity towards the advertised Aβ-42 target.



**The FastScan™ Phospho-Tau (Thr181) ELISA Kit #58537** detects human tau in plasma from the hTau P301S mouse model in as little as 50 μL of plasma.

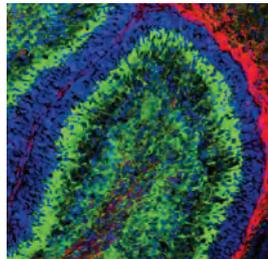
Data kindly provided by Dr. Li-Huei Tsai (Massachusetts Institute of Technology) and used with permission.

## Neuronal Markers

Studying the brain and nervous system requires examination not only of neurons, but also of microglia, oligodendrocytes, and astrocytes. The key to visualizing and identifying each of these cell types lies in using antibodies that target protein biomarkers specifically expressed and localized within these cells. Cell Signaling Technology (CST) provides highly specific, validated antibodies against accepted neuronal markers.

### Immature Neuronal Markers

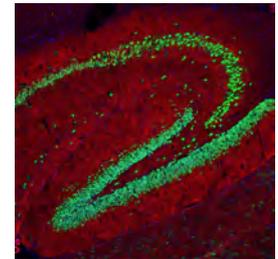
- Doublecortin
- NeuroD1
- TBR1
- $\beta$ 3-Tubulin



**Doublecortin (A8L1U) Rabbit mAb #14802:** Confocal IF analysis of P5 mouse cerebellum using #14802 (green), GFAP #3670 (red), and DRAQ5<sup>®</sup> #4084 (pseudocolor blue).

### Mature Neuronal Markers

- MAP2
- NeuN
- Neurofilament-H/L/M
- Neuron Specific Enolase (NSE)
- Tau
- Thy1
- $\beta$ 3-Tubulin



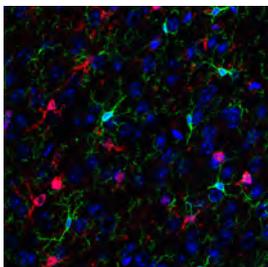
**NeuN (D4G4O) XP<sup>®</sup> Rabbit mAb #24307:** Confocal IF analysis of mouse hippocampus using #24307 (green) and actin labeled with DyLight<sup>™</sup> 554 Phalloidin #13054 (red). DRAQ5<sup>®</sup> (pseudocolor blue).

## Glial Markers

Glial cells consist of the non-neuronal supporting cells, including astrocytes, oligodendrocytes, and microglia. Distinct changes in glial cells and their markers are known to be associated with neurodegenerative disease progression. Glial cells also play an important role in overcoming challenges with the blood-brain barrier. CST has a wide variety of validated glial marker antibodies to identify and study the different glial cell types.

### Astrocytes

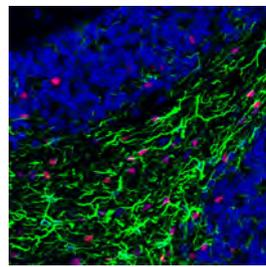
- GFAP
- S100B
- ALDH1L1
- AQP4
- EAAT1/2



**S100B (E7C3A) Rabbit mAb #90393:** Confocal IF analysis of fixed frozen mouse cerebral cortex. #90393 (red), HS1 (Alexa Fluor<sup>®</sup> 488 Conjugate) #68206 (green), and DAPI #8961 (blue).

### Oligodendrocytes

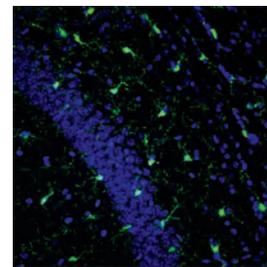
- MBP
- MOG
- Olig2
- CNPase
- PLP1



**Olig2 (E6G6Q) XP<sup>®</sup> Rabbit mAb #65915:** Confocal IF analysis of fixed frozen mouse cerebellum. #65915 (red), GFAP (Alexa Fluor<sup>®</sup> 488 Conjugate) #3655 (green), and DAPI #4083 (blue).

### Microglia

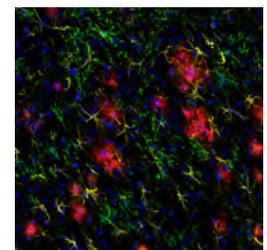
- Iba1
- CD11b
- CD45
- F4/80
- CD68



**Iba1/AIF-1 (E4O4W) XP<sup>®</sup> Rabbit mAb #17198:** Confocal IF analysis of mouse CA1 hippocampus using #17198 (green) and DAPI (blue). Images kindly provided by Dr. Marco Colonna (Washington University) and used with permission.

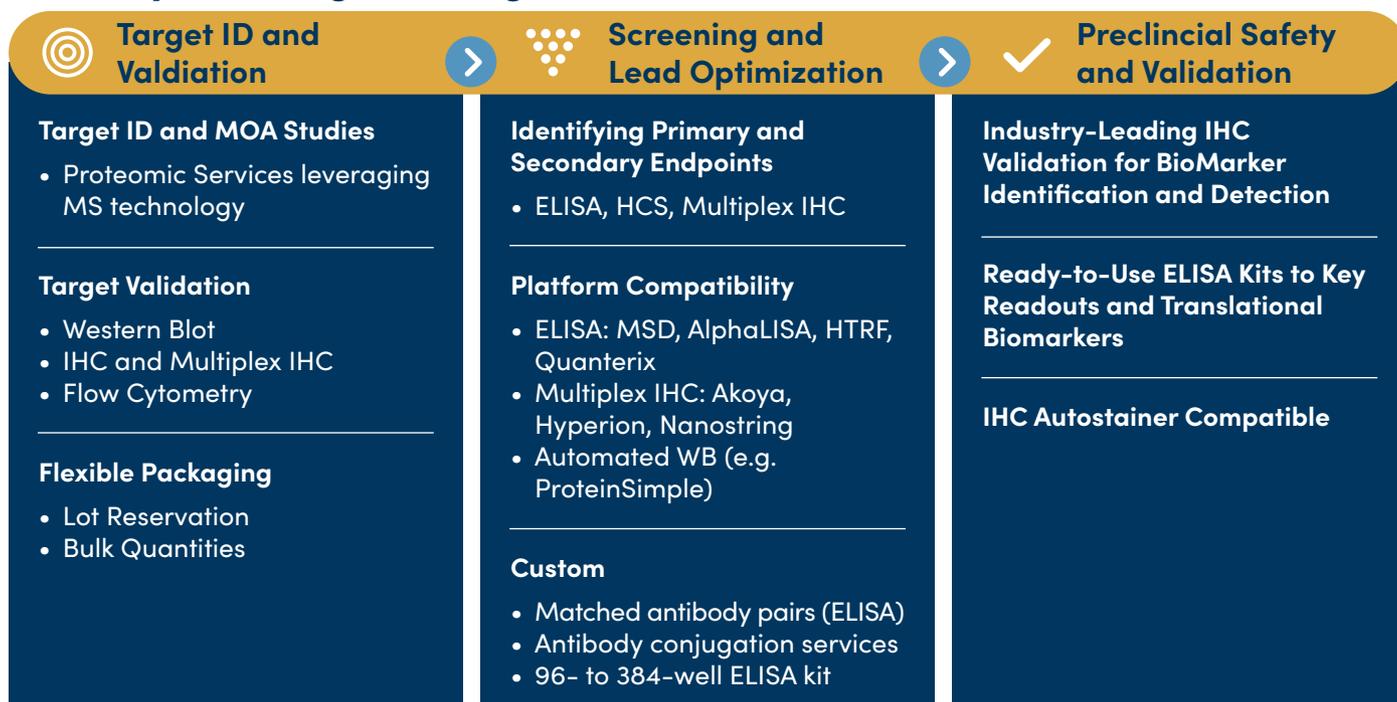
### DAM Markers

- ApoE
- DAP12 (TYROBP)
- TREM2
- GPNMB
- TMEM119
- Axl
- CD11c (ITGAX)/33
- Galectin-3



**TMEM119 (E3E1O) Rabbit mAb #90840:** Confocal IF analysis of an amyloid mouse model of Alzheimer's disease brain using #90840 (green), GFAP #3670 (yellow),  $\beta$ -Amyloid (Alexa Fluor<sup>®</sup> 647 Conjugate) #42284 (red), and DAPI #8961 (blue).

## Industry-Leading and Aligned to Your Workflow



## Antibodies That Work on Your Platform

Platforms	Application	Conjugate Type*	Product Format
<ul style="list-style-type: none"> <li>TR-FRET/LANCE/HTRF</li> <li>AlphaLISA/Screen</li> <li>MSD</li> <li>Quanterix (Simoa)</li> <li>Luminex</li> </ul>	<ul style="list-style-type: none"> <li>High Throughput ELISA</li> </ul>	<ul style="list-style-type: none"> <li>Fluorophores</li> <li>Lanthanides</li> <li>Biotin</li> <li>Beads</li> </ul>	<ul style="list-style-type: none"> <li>BSA- and Azide-Free Formulation</li> <li>Matched Antibody Pairs</li> <li>Optimized Concentration</li> </ul>
<ul style="list-style-type: none"> <li>CyTOF/Helios</li> <li>Hyperion</li> <li>MIBI</li> </ul>	<ul style="list-style-type: none"> <li>Flow Cytometry</li> <li>Mass Cytometry/IMC</li> <li>Multiplex IHC</li> </ul>	<ul style="list-style-type: none"> <li>Metal Ions</li> </ul>	
<ul style="list-style-type: none"> <li>Akoya</li> <li>Nanostring</li> <li>10 Genomics (Visium)</li> <li>Leica (Cell DIVE)</li> </ul>	<ul style="list-style-type: none"> <li>Multiplex IHC</li> </ul>	<ul style="list-style-type: none"> <li>Oligonucleotides</li> <li>Fluorophores</li> </ul>	<ul style="list-style-type: none"> <li>BSA- and Azide-Free Formulation</li> <li>Optimized Concentration</li> </ul>
<ul style="list-style-type: none"> <li>IHC Autostainers</li> </ul>	<ul style="list-style-type: none"> <li>IHC</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	
<ul style="list-style-type: none"> <li>High Content Screening &amp; Analysis</li> </ul>	<ul style="list-style-type: none"> <li>IF Imaging</li> </ul>	<ul style="list-style-type: none"> <li>Fluorophores</li> </ul>	
<ul style="list-style-type: none"> <li>ProteinSimple</li> </ul>	<ul style="list-style-type: none"> <li>Simple Western</li> </ul>	<ul style="list-style-type: none"> <li>N/A</li> </ul>	<ul style="list-style-type: none"> <li>Antibodies validated in house for Simple Western**</li> </ul>

\*Some conjugates directly available for purchase from CST (other conjugate types may be proprietary)

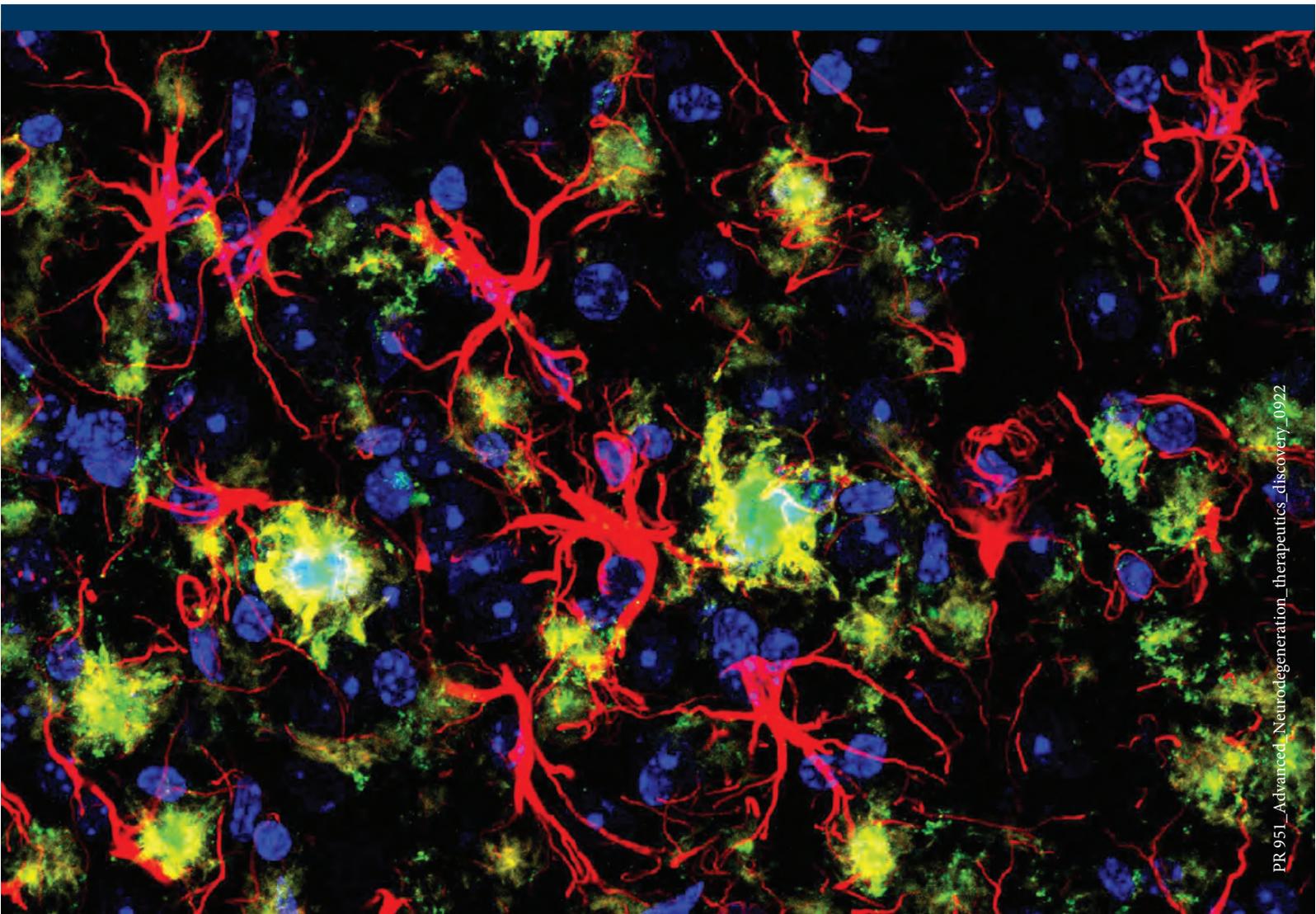
\*\*Growing list of select antibodies

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