Neuroinflammation

Research Products

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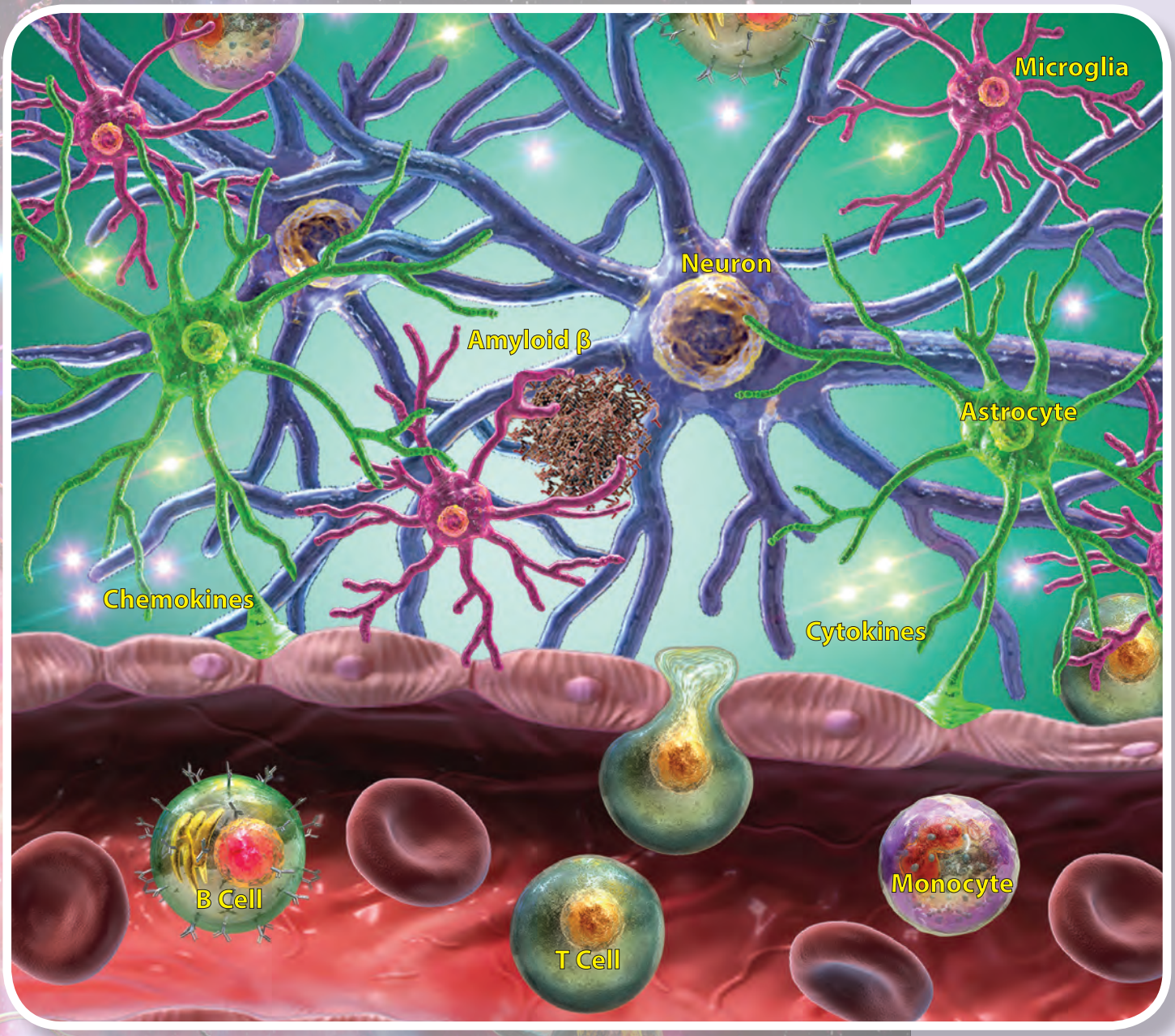

Introduction

Neuroinflammation refers to the inflammation of the nervous tissue, and is an immune response often initiated against a variety of harmful stimuli such as pathogens or trauma. Neuroinflammation is a complex biological response involving many signaling proteins, receptors, and cell types. A combination of responses from resident glial cells in the central nervous system (microglia, oligodendrocytes, and astrocytes), non-glial resident myeloid cells (macrophages and dendritic cells (DCs)), and peripheral leukocytes constitute the basis for neuroinflammation in the CNS.

Neuroinflammation plays an important role in many disorders of the nervous system and is a common component of many neurodegenerative diseases such as Alzheimer's (AD) and Parkinson's (PD) disease. Production of toxic protein aggregates and/or metabolites in these disorders is often associated with chronic inflammation and sustained activation of resident brain immune cells. This response ultimately leads to the production of inflammatory molecules, disruption of the blood-brain barrier (BBB), recruitment of peripheral immune cells, and amplification of the immune response. Ultimately, chronic inflammation culminates in a variety of responses such as aberrant synaptic pruning, axonal demyelination and degeneration, and eventual loss of neurons.

Acute neurotoxic insults such as trauma, on the other hand, can trigger the production of anti-inflammatory factors such as cytokines and chemokines by microglia, astrocytes and peripheral immune cells. These factors lead to the removal of neurotoxic insults, cellular repair and regeneration, and resolution of inflammation. A balance between pro- and anti-inflammatory responses determines whether the integrity of the BBB is maintained or disrupted, hence limiting the infiltration of peripheral immune cells into the brain which in turn can dampen or amplify the inflammatory signals leading to cell death or resolution of inflammation.

BioLegend offers a comprehensive portfolio of products, including antibodies, immunoassay solutions, and recombinant proteins, to interrogate inflammatory pathways in the CNS.

BioLegend Tools for Neuroinflammation Research

Purified & Conjugated Antibodies	Ultra Low Endotoxin, Azide-Free Antibodies for Bioassays	Recombinant Proteins	Immunoassay Solutions	MojoSort™ Magnetic Cell Separation
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Learn more at: biolegend.com/neuroinflammation

CNS Resident and Peripheral Immune Cells

The CNS houses a number of glial and non-glial cell types that work cooperatively and together with peripheral immune cells to counteract immune threats and maintain homeostasis. BioLegend provides solutions with utility in multiple applications to identify and study these cell types.

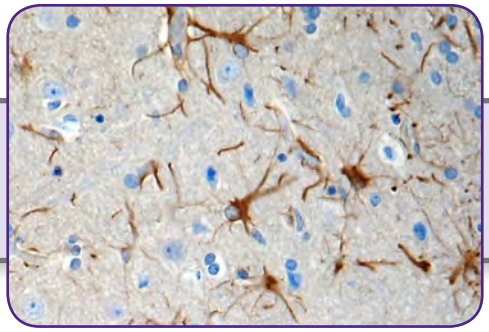
Visit our cell markers page: biolegend.com/cell_markers

CNS-Resident Glial Cells

Innate immune responses in the CNS can be initiated locally through the function of resident glial cells.

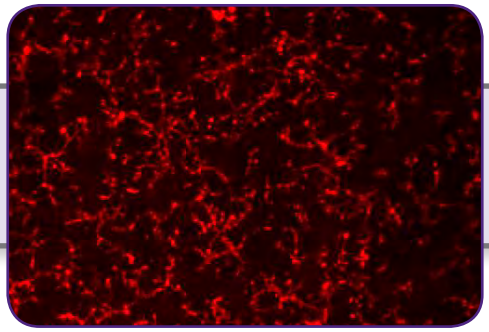
Microglia are the resident macrophages in the CNS, accounting for 10-15% of all cells found within the brain. Microglia can be identified using several common markers which they share with macrophages, such as CD11b, CD45, CD68 and CX3CR1. These cells also express specific markers such as P2RY12, which allow for their distinction from other cell types in the brain as well as peripheral immune cells. Using long branching processes, microglia actively survey their surrounding domain and can rapidly respond to environmental changes such as an immune threat. As a consequence, these cells undergo morphological changes to thicken and retract their processes, and take on an amoeboid shape and become phagocytic to remove the encountered threat. These morphological changes are also accompanied by expression and secretion of inflammatory molecules such as cytokines and chemokines, which help microglia communicate with astrocytes and peripheral immune cells.

CX3CR1



FFPE human AD brain tissue stained with anti-CX3CR1 antibody (clone 8E10.D9).

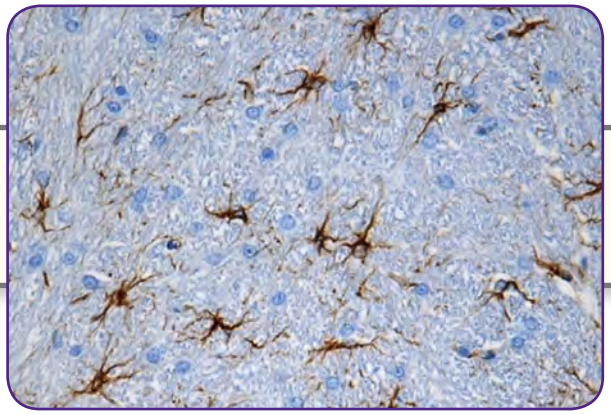
P2RY12



PFA-fixed frozen mouse brain tissue stained with anti-P2RY12 antibody (clone S16007D).

Astrocytes are the most abundant glial cell type in the brain, accounting for 20 to 40% of all glial cells, and can be identified with markers such as GFAP and S100β. Astrocytes are commonly known to possess a star-shaped morphology with fine, elaborate processes. These cells perform many functions such as providing metabolic support for neurons (*e.g.* they produce and secrete glutamine and lactate) as well as rapidly removing excess neurotransmitter (*e.g.* glutamate) released into the synaptic cleft to protect neurons against neurotoxicity. In addition, astrocytes help in the maintenance of the BBB integrity and permeability by projecting astrocytic endfeet to encircle and cover endothelial cells of the blood vessels, which together with the parenchymal basal lamina form the glia limitans. Similar to microglia, astrocytes are highly sensitive to alterations in their microenvironment. In response to CNS injury, they undergo morphological changes and alter their gene expression profile to upregulate expression and secretion of a variety of bioactive molecules, such as cytokines and chemokines. Furthermore, the function of astrocytes in the maintenance of the BBB has significant implications during inflammation, as dysfunction of astrocytes may lead to BBB disruption and favor the infiltration of peripheral immune cells and molecules into the CNS.

GFAP



FFPE rat brain tissue stained with anti-GFAP antibody (clone SMI 24).

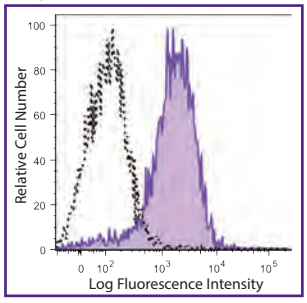
Oligodendrocytes (ODs) are a type of glial cell that produce myelin sheath to allow insulation of segments of neuronal axons and enable high velocity signal transduction essential for the propagation of action potentials along the axon. ODs also contribute to neuroplasticity and provide trophic support to neurons by producing factors such as glial cell line-derived neurotrophic factor (GDNF). Each OD can extend its processes to multiple axons and has a great capacity to rapidly renew its myelin sheaths. As a result, ODs have a high metabolic rate and are highly vulnerable to oxidative stress. The latter is also partly due to relatively low levels of anti-oxidative enzymes in ODs. Microglia produce various pro-inflammatory mediators that can induce bystander damage to their neighboring glial cells and neurons. As a consequence of their high metabolic activity, oligodendrocytes are more susceptible to these factors and respond by producing poor quality myelin, which may ultimately lead to the loss of OD-neuron connections and axon degeneration. Damaged ODs can also initiate pathways of cell death, which can further activate microglia and amplify the inflammatory cascade. Myelin basic protein (MBP), myelin CNPase, and CD140a are specific markers that allow identification of oligodendrocytes.

CNS-Resident Non-Glial Cells

The CNS contains macrophages and DCs that are non-microglial myeloid cells localized to perivascular space, choroid plexus, and meninges. These cells act as effector and regulatory cells for the immune response at the CNS borders. DCs are professional antigen-presenting cells that act as sentinels of the immune system by constantly surveying their environment for potentially harmful pathogen- or self-derived molecules. Thus they serve as a bridge between adaptive and innate immune systems. Similar to DCs, macrophages function in local immune surveillance and phagocytosis of cellular and pathogenic debris. Under neuroinflammatory conditions, macrophages and DCs infiltrate the brain parenchyma in response to inflammation-induced cytokines and chemokines, and help augment pro- or anti-inflammatory responses initiated by the resident immune cells of the brain. Macrophages can be identified using a combination of surface markers such as CD11b, CD68, and F4/80 in mice. Conventional DCs can be defined as B220^{-} CD11c^{+} CD45^{hi} MHC Class II^{hi} in mice, whereas CD11c and CD141 markers are often used in human samples.

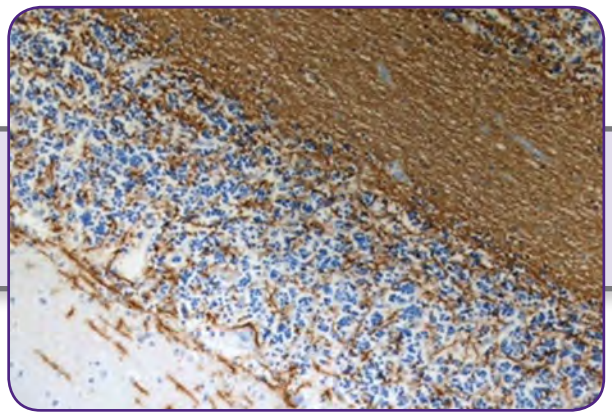
A comprehensive list of CD (or cluster of differentiation) products for immune cell types can be found at:
biolegend.com/cdchart
biolegend.com/essential_markers
biolegend.com/cell_markers

F4/80



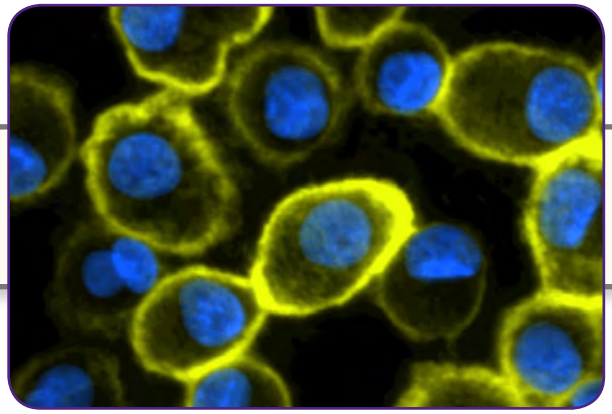
Thioglycolate-elicited mouse peritoneal macrophages stained with APC/Fire™ 750 anti-mouse F4/80 antibody (clone BM8, filled histogram) or APC/Fire™ 750 rat IgG2a, κ isotype control (open histogram).

Myelin Basic Protein



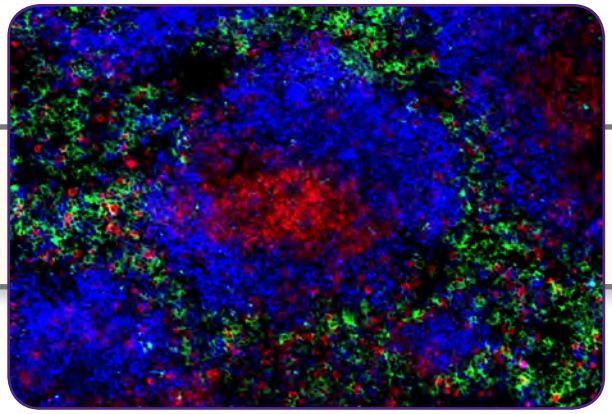
FFPE human cerebellum tissue stained with anti-Myelin Basic Protein antibody (clone SMI 94).

CD11c



Human peripheral blood mononuclear cell (PBMC)-derived dendritic cells stained with Brilliant Violet 510™ anti-human CD11c antibody (clone 3.9, yellow). Nuclei were counterstained with DAPI (blue).

F4/80



Frozen mouse spleen section co-stained with Alexa Fluor® 488 anti-mouse F4/80 (clone BM8, green), Brilliant Violet 510™ anti mouse/human CD45R/B220 (clone RA3-6B2, blue) and Brilliant Violet 421™ anti-mouse CD3 (clone 17A2, red) antibodies.

CNS-Resident Glial Cell Marker Antibodies

	Specificity	Clone	Reactivity	Application (s)
Microglia	CD11b	CBRM1/5	Hu	IP, FC
		ICRF44	Hu, NHP	IHC, ICC, FC, CyTOF®
		M1/70	Hu, Ms, NHP	IHC-F, ICC, IP, FC, CyTOF®
	CD45	2D1	Hu	IHC-P, FC
		HI100	Hu, NHP	IHC-F, IHC-P, ICC, FC, CyTOF®
		HI30	Hu, NHP	WB, IHC-P, FC, CyTOF®
		MEM-55	Hu	WB, IHC-P, IP, FC
		RA3-6B2	Hu, Ms, Cat	ICH-F, ICC, IP, FC, CyTOF®
		Tü116	Hu, NHP	FC
	CD68	FA-11	Ms	WB, IHC-F, IP, FC, ICFC
		KP1	Hu	WB, IHC-P, IP
		Y1/82A	Hu	ICC, ICFC
	Chil3/Ym1	A17046B	Ms	WB
	CX3CR1	2A9-1	Hu	FC
		8E10.D9	Hu	WB, IHC-P
		K0124E1	Hu, NHP	FC
		SA011F11	Ms	FC
	P2RY12	S16007D	Ms	IHC-P, FC
		S16001E	Hu	FC
	P2X7R	1F11	Ms	FC
	Siglec-H	551	Ms	FC
	MerTK	2B10C42	Ms	FC
		A311F9G3E1	Hu	WB
	TMEM119	A16075D	Hu	WB, ICC, FC
Astrocytes	GFAP	15C7D5D2	Hu	WB, ELISA
		2E1.E9	Hu, Ms, Rat	WB, IHC-P, ICC, FC
		Poly28294	Hu, Ms, Rat	WB, IHC-P, ICC
		SMI 21	Hu, NHP, Canine	WB, IHC-P, ICC
		SMI 22	Hu, Ms, Rat	WB, IHC-P, ICC
		SMI 23	Hu, Ms, Rat	WB, IHC-P
		SMI 24	Hu, Ms, Rat	WB, IHC-P
		SMI25	Hu, Ms, Rat	WB, IHC-P
		SMI 26	Hu, Ms, Rat	WB, IHC-P, ICC
	Glutamine Synthetase	O91F4	Hu, Ms, Rat	WB, IHC-P
	S100B	11C12E12	Hu, Ms, Rat	WB
Oligodendroycyte	A2B5	105	Hu, Ms	FC
	MAG	B11F7	Human, Mouse, Rat	WB, IHC-P
	Myelin Basic Protein	P82H9	Hu, Rat	WB, IHC-P
		SMI 94	Hu, Ms, Rat	WB, IHC-P
		SMI 99	Hu, Ms, Rat	WB, IHC-P
	Myelin CNPase	SMI 91	Mammalian	WB, IHC-P
	PDGFRα (CD140a)	16A1	Hu	FC
		APA5	Ms	FC

CNS Resident Non-Glial Cell Marker Antibodies

	Specificity	Clone	Reactivity	Application (s)
Macrophages	CD11b	CBRM1/5	Hu	IP, FC
		ICRF44	Hu, NHP	IHC, IF, FC, CyTOF®
		M1/70	Hu, Ms, NHP	IHC, IF, IP, FC, CyTOF®
	F4/80	BM8	Ms	IHC, FC
	CD68	FA-11	Ms	WB, IHC, IP, FC, ICFC
		KP1	Hu	WB, IHC, IP
		Y1/82A	Hu	IHC, IF, ICFC
	CD163	GHI/61	Hu, NHP	WB, ICC, IP, FC
		RM3/1	Hu	IF, FC
Dendritic Cells	CD11c	3.9	Hu, NHP	IHC, FC, CyTOF®
		Bu15	Hu	FC, CyTOF®
		N418	Ms	IHC, IP, FC, CyTOF®
		S-HCL-3	Hu	IHC, IP, FC
	CD45R/B220	RA3-6B2	Hu, Ms, Feline	IHC, IP, FC, CyTOF®
	CD141	M80	Hu	FC
		Phx-01	Mammalian	WB, IHC, ELISA
	MHC Class II	L243	Hu, NHP	WB, IHC, IP, FC, CyTOF®
		M5/114.15.2	Ms	IHC, IP, FC
		Tü39	Hu	IP, FC

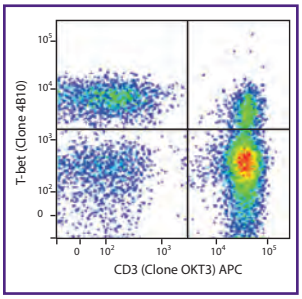
CyTOF® = Mass Cytometry, **FA** = Functional Assay, **FC** = Flow Cytometry, **ICC** = Immunocytochemistry, **ICFC** = Intracellular Staining for Flow Cytometry, **IF** = Immunofluorescence Microscopy, **IHC** = Immunohistochemistry, **IHC-P** = Immunohistochemistry, paraffin embedded sections, **IHC-F** = Immunohistochemistry, frozen sections **IP** = Immunoprecipitation, **Neut** = Neutralization, **RIA**= Radio Immunoassay, **WB** = Western Blotting

Peripheral Immune Cells

Peripheral immune cells, including T lymphocytes, play an important role in CNS disorders such as multiple sclerosis (MS). These cells gain entry into the CNS parenchyma when the integrity of the BBB is compromised, and participate in regulating the outcome of neuroinflammation through releasing a variety of soluble factors such as cytokines. In experimental autoimmune encephalomyelitis (EAE), which is an animal model equivalent of MS, different subpopulations of $CD4^+$ T helper cells, Th1 and Th17, strongly contribute to chronic neuroinflammation. In contrast, regulatory T cells (Tregs) decrease inflammation and promote a neuro-supportive environment.[1] T cell subpopulations can be distinguished using a number of intra- and extra-cellular markers.

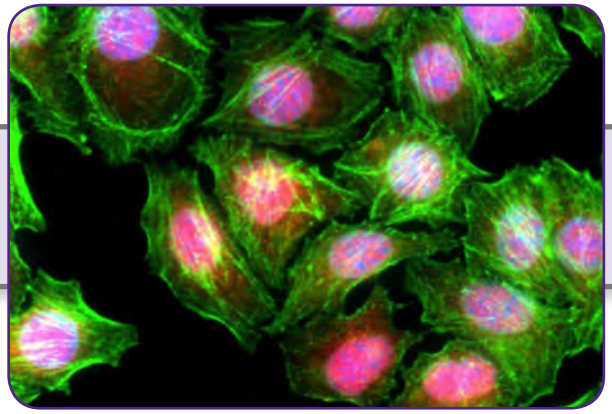
Visit BioLegend's T helper page to learn more about T helper cell subsets: biolegend.com/thelper

T-bet



Human peripheral blood lymphocytes were surface stained with APC anti-CD3 antibody (clone OKT3) and then treated with True-Nuclear™ Transcription Factor Buffer Set. The cells were then stained with purified anti-T-bet antibody (clone 4B10) followed by anti-mouse IgG1 PE.

STAT4



HeLa cells stained with anti-STAT4 Antibody (clone 15A1B41, red) and Alexa Fluor® 488 Phalloidin (green). Nuclei were counterstained with DAPI (blue).

Th1 Cell Marker Antibodies

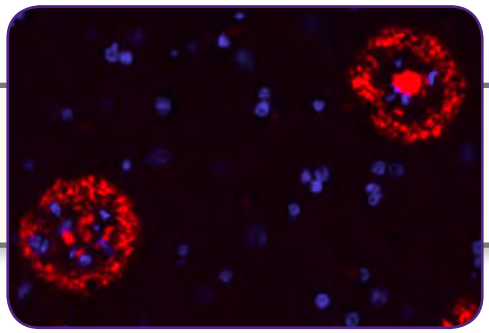
	Specificity	Clone	Reactivity	Application (s)
Intracellular Markers†	IL-2	JES6-1A12	Ms	WB, IP, ELISA Capture
		JES6-5H4	Ms	IHC, IP, ICFC, ELISA Capture
		MQ1-17H12	Hu, NHP	IHC, IP, ELISA Capture, CyTOF®
	STAT1	10C4B40	Hu	WB
	STAT1 Phospho (Ser727)	A15158B	Hu, Ms	WB, IF, ICFC
	STAT4	15A1B41	Hu, Ms	WB, IF, IP
	T-bet	4B10	Hu, Ms	WB, IF, IP, ICFC
Extracellular Markers†	CD3‡	17A2	Ms	IHC, IP, FC
		1F4	Rat	IHC, FC
		BC3	Hu	FC
		HIT3a	Hu	IHC, IP, FC
		SK7	Hu, NHP	WB, IHC, IF, FC
		UCHT1	Hu, NHP	WB, IHC, IP, FC, CyTOF®
	CD4‡	A161A1	Hu	FC
		GK1.5	Ms	IHC, IP, FC
		H129.19	Ms	IHC, FC
		OKT4	Hu, NHP	IHC, FC
		W3/25	Rat	IHC, FC
	CD195 (CCR5)	J418F1	Hu	FC
		HEK/1/85a	Hu	FC
		HM-CCR5	Ms	FC
	CD218a (IL-18Rα)	BG/IL18RA	Ms	FC
		H44	Hu	IHC, FC
	CD366 (Tim-3)	B8.2C12	Ms	FC
		F38-2E2	Hu, NHP	FC
		RMT3-23	Ms	IHC, FC

‡Additional clones available
†Additional cell markers available

Innate Immunity in Neuroinflammation: The Role of Microglia in Alzheimer's disease

Increasing evidence implicates activation and function of microglia as a cardinal feature of many neurodegenerative disorders including Alzheimer's disease. However, it is not clear whether microglia-mediated neuroinflammation plays a beneficial or detrimental role in disease. In AD brain tissues, microglia are found in abundance surrounding amyloid plaques. Furthermore, genetic mutations or variants in immune-related proteins, such as Triggering Receptor Expressed on Myeloid cells 2 (TREM-2) being expressed on microglia, have shown to be a risk factor in developing AD.[2,3]

β-Amyloid, 1-16



FFPE human AD brain tissue stained with Alexa Fluor® 594 β-Amyloid, 1-16 antibody (clone 6E10, red). Nuclei were counterstained with DAPI (blue).

Microglia express a number of surface receptors including pattern recognition receptors (PRRs) such as scavenger (*e.g.* CD36) and Toll-like receptors (TLRs) (*e.g.* TLR4, TLR6) capable of mounting an inflammatory response upon encountering exogenous or host-derived stress signals to counteract these insults. Amyloid beta (Aβ), a major component of amyloid plaques deposited in the brains of AD patients, binds to and triggers activation of intracellular signaling cascades that lead to induction of inflammatory responses and/or phagocytic activity by microglia. Such activity is observed through cooperation between three microglial PRRs: CD36, TLR4 and TLR6. CD36-mediated recognition of Aβ leads to the assembly of a hetero-trimeric complex composed of CD36-TLR4-TLR6, and propagation of TLR4-TLR6 signaling through adaptor proteins MyD88 and TRIF. This signaling event leads to the activation of NF-κB-dependent expression of proinflammatory genes, such as pro-IL-1β and NLRP3.[4] Maturation of pro-IL-1β into IL-1β requires formation of inflammasomes which act as an intracellular sensor for stress signals such as misfolded proteins. Assembly of an inflammasome in response to Aβ requires the oligomerization of NLRP3, recruitment of ASC and pro-caspase-1, and activation of caspase-1. Activated caspase-1, in turn, cleaves pro-IL-1β to produce active IL-1β.[4] In addition to its role in the hetero-trimeric complex, CD36 may directly mediate the uptake and internalization of Aβ into lysosomal compartments, where it forms fibrillar aggregates leading to lysosomal rupture, release of cathepsin B, and additional formation of inflammasomes and IL-1β production.[5] Of note, Aβ-induced secretion of IL-1β appears to be a critical component of microglial inflammatory response as elevated amounts of this cytokine have been detected in the brains and cerebrospinal fluids (CSF) of AD patients.[6] Thus, formation of inflammasomes and IL-1β production by microglia may mediate harmful inflammatory responses contributing to AD pathology.

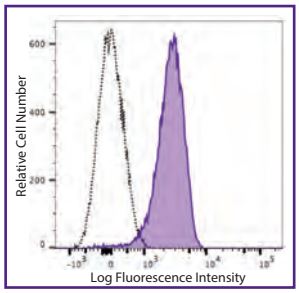
The complement system and its components play a prominent role in the inflammatory responses in AD. High levels of complement receptor 1 (CR1), which binds to complement factor C3b, have been detected in the CSF of AD patients.[7] Furthermore, polymorphisms in the CR1 gene are a risk factor associated with AD and correlate with increased levels of Aβ in the CSF.[7] Complement proteins are synthesized by diverse cell types in the CNS including microglia. Increased CR1 expression levels coupled to enhanced superoxide, TNF-α, and IL-1β production in activated microglia induce neuronal cell death, pointing to detrimental effects of complement system activation in these cells.

Single-cell RNA sequencing (RNA-seq) has enabled characterization of immune cell types under normal and disease conditions. This technique is highly useful in disorders with an inflammatory component where numerous cell types may be involved in disease pathology and/or resolution, highlights the heterogeneity and complexity of these cells in the CNS, and underscores the necessity of identifying unique cellular markers to distinguish these cell types.

Recently, using single-cell RNA-seq analysis, a novel population of microglia termed disease-associated microglia (DAM) has been identified in an AD-like mouse model.[8] Gene expression levels corresponding to homeostatic state of microglia, including P2RY12, CX3CR1 and TMEM119, were shown to be down-regulated in DAM. In contrast, expression of genes involved in phagocytic and lipid metabolism pathways,

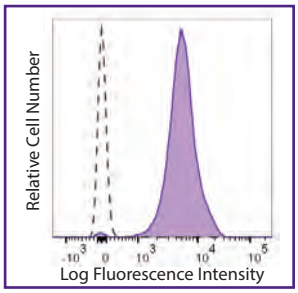
P2RY12

Human peripheral blood platelets stained with PE anti-P2RY12 antibody (clone S16001E, filled histogram) or PE mouse IgG2a, κ isotype control (open histogram).



CD36

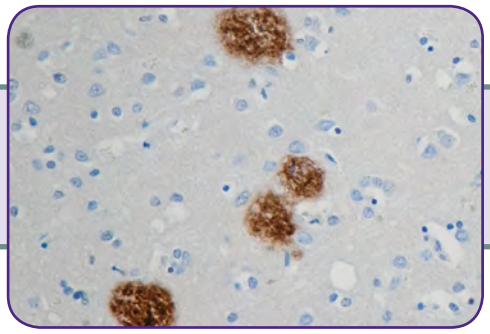
Human peripheral blood platelets stained with APC/Fire™ 750 anti-human CD36 antibody (clone 5-271, filled histogram) or APC/Fire™ 750 mouse IgG2a, κ isotype control (open histogram).



Aβ recognition, uptake and signaling in microglia. Aβ binds to several receptors expressed by microglia. The interaction between Aβ and CD36 initiates the assembly of CD36-TLR4-TLR6 complex, activation of NF-κB-dependent transcription of pro-IL-1β and its maturation into IL-1β through the assembly of the inflammasome complex. Aβ also binds to apolipoproteins ApoE and ApoJ forming complexes that are recognized by TREM-2. This interaction helps facilitate the uptake and degradation of Aβ by microglia. CR1 mediates phagocytosis and clearance of C3b-opsonized Aβ.

including AD risk factors such as TREM-2 and ApoE, were found to be up-regulated in these cells. DAM localize in the proximity of Aβ plaques and immunohistochemically, the majority of DAM stain positively with intracellular Aβ particles. These findings coupled to enhanced phagocytic activity suggest that DAM actively participate in the uptake and clearance of Aβ aggregates. Interestingly, TREM-2 is a transmembrane glycoprotein and acts as a sensor for a distinct set of lipoproteins and apolipoproteins notably ApoE and ApoJ (clusterin), which are apolipoproteins capable of binding to Aβ. This interaction helps facilitate the uptake and degradation of Aβ by the microglia.[3] In addition, TREM-2 variants found in AD patients demonstrate reduced ability to bind Aβ-apolipoprotein complexes. These findings underscore the involvement of the innate immune cells such as microglia in the clearance of Aβ aggregates, and their dysfunction as a predisposing risk factor for developing late onset AD.

ApoE4



FFPE human AD brain tissue stained with anti-ApoE4 antibody (clone 5A9).

To learn more about BioLegend's neuroinflammation products visit: biolegend.com/neuroinflammation

Visit our page on Amyloid Precursor Protein and Aβ to learn about APP processing and Aβ generation: biolegend.com/amyloid_precursor_protein

APP & Amyloid β Antibodies‡

Specificity	Clone	Reactivity	Application (s)
β-Amyloid, 1-11	NAB 228	Hu	WB, IHC-P, IP, ELISA Detection
β-Amyloid, 1-15	3A1	Hu	IHC-F, IHC-P, Direct ELISA
β-Amyloid, 1-16	6E10	Hu	WB, IHC-P, Direct ELISA
β-Amyloid, 1-38	7-14-4	Hu	WB, IHC-P, Direct ELISA
β-Amyloid, 1-40	11A50-B10	Hu, Ms, Rat	WB, IHC-P, IP
β-Amyloid, 1-42	12F4	Hu, Ms, Rat	WB, IHC-P, Direct ELISA
β-Amyloid, 17-24	4G8	Hu	IHC-P, Direct ELISA
β-Amyloid, aggregated	A17171C	Hu	IHC-P
β-Amyloid Pyroglutamyl (Glu3)	337.48	Hu, Ms, Rat	WB, IHC-P
APP	LN27	Hu	WB

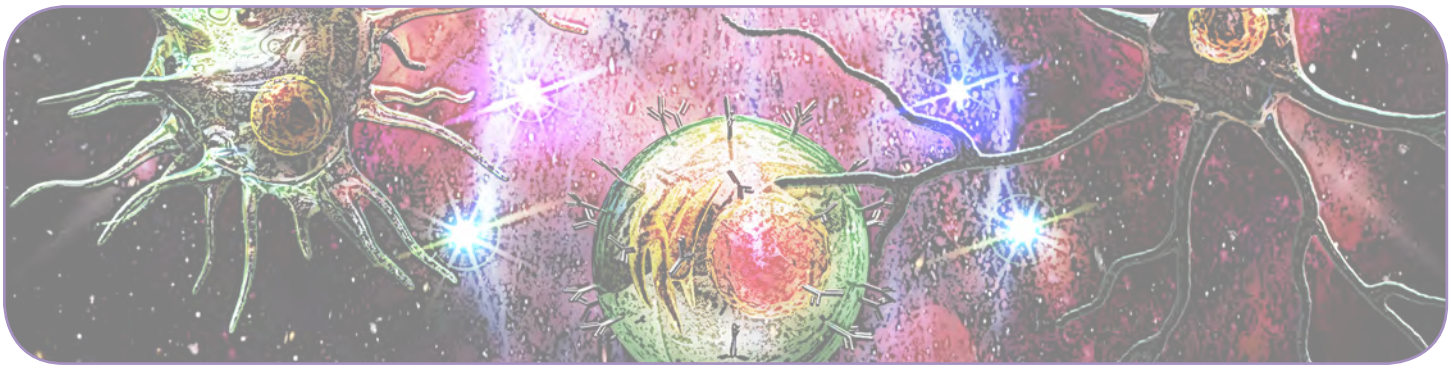
Pattern Recognition Receptor Antibodies

	Specificity	Clone	Reactivity	Application (s)
Scavenger Receptors	CD36	5-271	Hu	IHC, IF, FC
		HM36	Ms	FC
	CD36 (SCARB1, SR-BI)	m1B9	Hu	FC
	CD204 (MsR1)	7C9C20	Hu	FC
		7G5C33	Ms	WB
	LOX-1 (SCARE1)	15C4	Hu	IHC, FC
Toll-Like Receptors	TLR1 (CD281)	TLR1.136	Hu	IF, IP, FC
	TLR2 (CD282)	CB225	Ms	FC
		QA16A01	Hu, Ms	FC, Block
		TL2.1	Hu	WB, IHC, IP, FC
	TLR3 (CD283)	11F8	Ms	IHC, ICFC
		TLR-104	Hu	WB, ICFC
	TLR4 (CD284)	HTA125	Hu, Guinea Pig	IHC, IF, FC
		SA15-21	Ms	IP, FC
	TLR4 (CD284)/MD2 Complex	MTS510	Ms	WB, IHC, IF, IP, FC
	TLR5 (CD285)	ACT5	Ms	IP, FC
	TLR6 (CD286)	TLR6.127	Hu	FC

TLR Signaling Protein Antibodies

Specificity	Clone	Reactivity	Application (s)
CD14	63D3	Hu	FC
	HCD14	Hu	IF, FC
	M14-23	Ms	FC
	M5E2	Hu, NHP	IHC, IF, FC, CyTOF®
	Sa14-2	Ms	FC
IκB-α	3D6C02	Hu	WB, IF
MyD88	O91B8	Hu	WB
TRAF6	T2-1SC	Hu, Ms	WB
NF-κB (p50)	4D1	Hu	WB, IF
NF-κB (p65)	14G10A21	Hu	WB, IP
	Poly6226	Hu, Ms, Rat	WB, IHC, IF, IP
TICAM-1 (TRIF)	1H4B01	Hu, Ms	WB, IF, IP
TICAM-2 (TRAM)	9G1B30	Hu	WB

‡Additional clones available



Inflammasome-Related Protein Antibodies

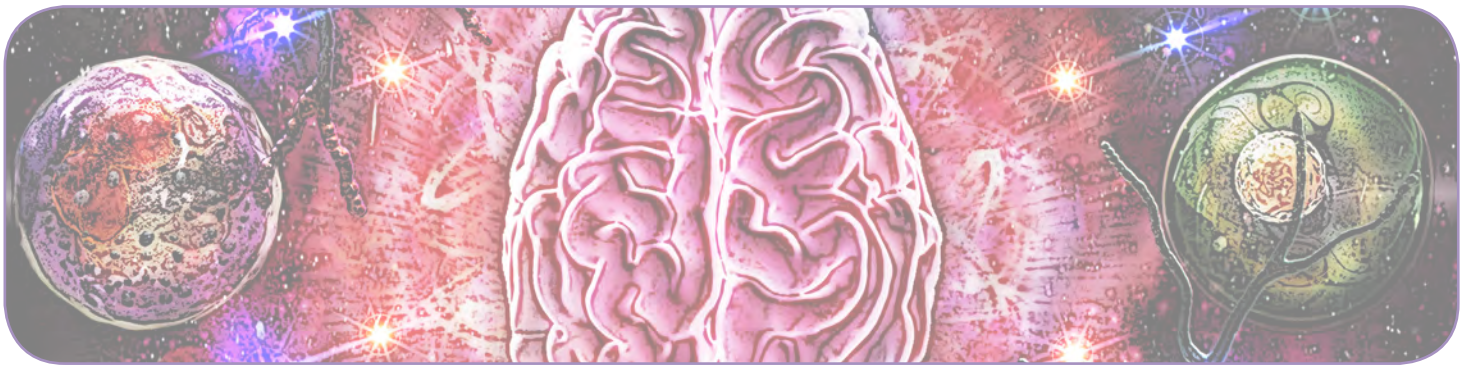
Specificity	Clone	Reactivity	Application (s)
ACS (TMs-1)	HASC-71	Hu	WB, IF, IP
	O93E9	Hu	WB
AIM2	3B10	Hu	WB, IF, IP
Caspase-1	5B10	Ms	WB, IHC
Cathepsin B	15D10C39	Hu	WB
NLRC4	6H9B13	Hu	WB, IF
NLRP1	9F9B12	Hu	WB

Phagocytic & Lipid Metabolism Protein Antibodies

Specificity	Clone	Reactivity	Application (s)
ApoE	3B3C32	Ms	WB
	D6E10	Hu	WB, IHC, IP, ELISA
	E6D7	Hu	WB, IHC, IP, ELISA
ApoE4	5A9	Hu	IHC, ELISA
	5B5/ApoE4	Hu	IHC, ELISA
	5G7	Hu	WB, ELISA
	9D11	Hu	WB, ELISA
ApoJ (Clusterin)	A15113A	Hu	WB, IHC, ELISA
	Poly18133	Hu	WB, IHC, ELISA
LRP2	CD7D5	Hu, Ms, Rat	IHC, IF
LRP4	N207/27	Ms, Rat	WB
TREM-1 (CD354)	TREM-26	Hu, Canine	WB, FC
	TREM27	Hu	WB, FC, ELISA Capture

Complement Protein & Receptor Antibodies

	Specificity	Clone	Reactivity	Application (s)
Complement Proteins	C3/C3b/iC3b	6C9/C3b	Hu	WB, FC, ELISA
		7C12/C3b	Hu	IF, FC, ELISA, RIA
	C3/C3b/iC3b/C3d	1H8/C3b	Hu	WB, IF, FC, ELISA
	C3a/C3a(desArg)/C3	D17/1	Hu	WB, ELISA Capture
		K13/16	Hu	WB, IP, ELISA Capture
	C3b/iC3b	3E7/C3b	Hu, NHP	IF, FC, ELISA, RIA
	C5a/C5a(desArg)	C17/5	Hu	WB, ELISA Capture
	C5a/C5a(desArg)/C5	G25/2	Hu	WB, IP, ELISA Detection
	Factor H	C18/3	Hu	WB, ELISA Capture
		L20/3	Hu	WB, ELISA Detection
Complement Receptors	C5L2	1D9-M12	Hu	WB, FC
	CD88 (C5aR)	20/70	Ms	FC
		S5/1	Hu	FC
	CR1 (CD35)	E11	Hu	IHC, IP, FC
	CR2 (CD21)	Bu32	Hu	FC
	CR3 (CD11b/c)	OX-42	Rat	IHC, IP, FC



Adaptive Immunity in Neuroinflammation: The Role of Regulatory T cells in Neurological Autoimmune Disorders

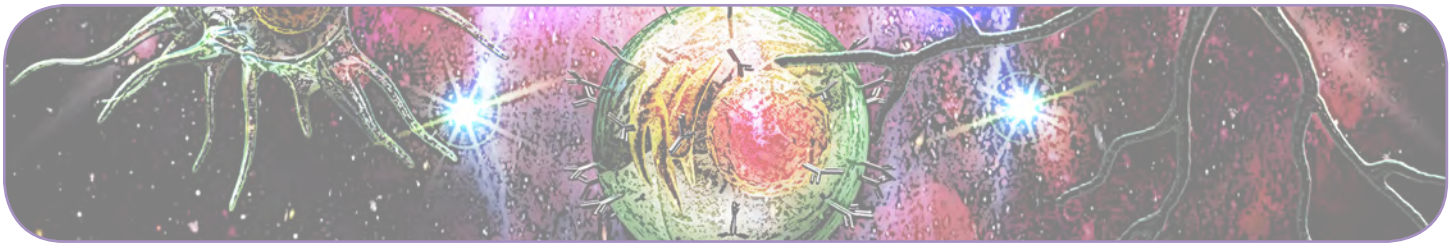
Maintaining the balance between effector T cells and suppressive regulatory T cells is important in the development of autoimmune disorders. An imbalance favoring effector cells can often lead to a hyperactive immune system resulting in inflammation, tissue damage and destruction. Such is the case for MS, which is a debilitating autoimmune disease of the CNS mediated partly by T lymphocytes autoreactive to myelin. In MS patients, an increase in the number of effector Th1 and Th17 cells, and elevated levels of pro-inflammatory cytokines (*e.g.* IL-1, IL-6, TNF-α) have been reported. Furthermore, lower thymic production of Treg cells and a decreased diversity in the T cell receptor (TCR) repertoire attributed to defects in transforming growth factor beta (TGF-β) signaling has been observed in MS patients.[9] TGF-β, a highly expressed cytokine in the CNS, has been shown to positively regulate the differentiation of naïve $CD4^+$ T cells into $CD4^+$ $CD25^+$ $FOXP3^+$ Treg cells, and lead to adequate recognition and suppression of immune responses to self-proteins such as myelin. In contrast to myelin sheath damage caused by CNS infiltrating effector T cells, Treg cells demonstrate regenerative properties, and have emerged as mediators of oligodendrocyte differentiation and (re)myelination, thus promoting tissue regeneration and resolution of inflammation.[10] These findings highlight the cooperative function of signaling molecules and immune cells in regulating the immune response and prevention of disease development.

Learn more about Tregs at: biolegend.com/treg

Treg Marker Antibodies

	Specificity	Clone	Reactivity	Application (s)
Transcription Factors	FOXP3	150D	Hu, Ms, Rat, NHP	WB, ICFC
		206D	Hu, NHP	WB, IHC, ICFC
		259D	Hu, NHP	WB, IHC, ICFC
		MF-14	Ms	WB, ICFC
		Poly6238	Hu, Ms	WB, IHC
	Helios	22F6	Hu, Ms	ICFC
Extracellular Markers†	CD4	A161A1	Hu	FC
		GK1.5	Ms	IHC, IP, FC
		H129.19	Ms	IHC, FC
		OKT4	Hu, NHP	IHC, FC
		RM4-4	Ms	FC
		RM4-5	Ms	IHC, FC, CyTOF®
		RPA-T4	Hu, NHP	IHC, FC, CyTOF®
		SK3	Hu	IP, FC
		W3/25	Rat	IHC, FC
	CD25	3C7	Ms	IHC, FC, CyTOF®
		BC96	Hu, NHP	IF, FC
		M-A251	Hu, NHP	IHC, FC
		PC61	Ms	IHC, IP, FC
	CD134 (OX40)	Ber-ACT35 (ACT35)	Hu, NHP	WB, IHC, FC, ELISA, CyTOF®
		OX-40	Rat	FC
		OX-86	Ms	FC
	CD152 (CTLA-4)	9H10	Ms	ELISA, FC
		A3.6B10.G1	Hu	ELISA Capture
		BNI3	Hu	FC
		L3D10	Hu	FC
		UC10-4B9	Ms	IP, FC, ELISA
	CD194 (CCR4)	2G12	Ms	FC
		L291H4	Hu	FC

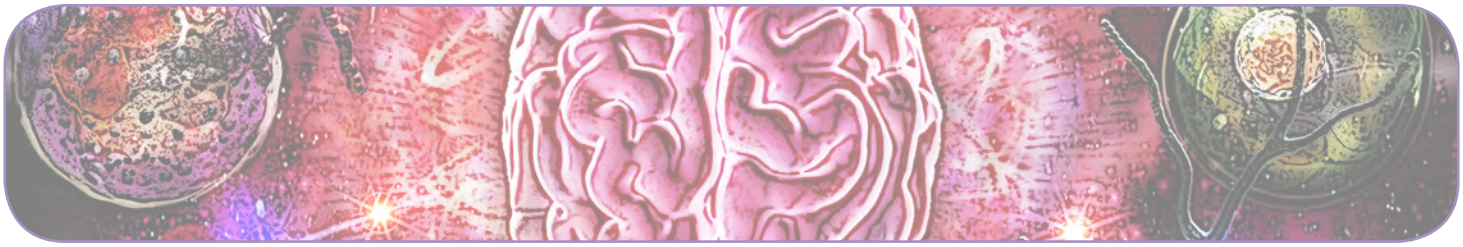
†Additional extracellular markers available



Cytokine Antibodies†

Specificity	Clone	Reactivity	Application (s)
IL-1β	H1b-27	Hu	ELISA Capture
IL-5	JES1-39D10	Hu, NHP	WB, IHC, ELISA Capture
	JES1-5A10	Hu, NHP	ELISA Capture
	TRFK5	Hu, Ms, Guinea Pig	WB, IHC, ELISA Capture, CyTOF®
IL-6	MP5-20F3	Ms	IHC, ELISA Capture, CyTOF®
	MP5-32C11	Ms	ELISA & ELISPOT Detection
	MQ2-13A5	Hu	ELISA Capture, CyTOF®
	MQ2-39C3	Hu	WB, ELISA
	Poly5177	Rat	ELISA Capture
IL-10	JES3-12G8	Hu	IHC, ICFC, ELISA
	JES3-19F1	Hu	WB, IHC, ELISA Capture
	JES3-9D7	Hu, NHP	IHC, ELISA Capture
	JES5-16E3	Ms	IHC, ELISA Capture, CyTOF®
	JES5-2A5	Ms	WB, ELISA Capture
	MK10A6	Ms	ELISA Capture
IL-12 (p70)	7B12	Hu	ELISA Capture
	C18.2	Ms	ELISA Capture
IL-17A	BL168	Hu	ICFC
	BL23	Hu	ELISA Capture
	TC11-18H10.1	Ms	WB, ICFC, ELISA Capture, ELISPOT, CyTOF®
IL-17F	6B9.H8	Hu, Ms	WB
IL-18	KU18-81	Hu	WB
IL-22	BL35175	Hu, Ms	WB
	Poly5161	Hu	ELISA Capture
	Poly5164	Ms	ELISA Capture
IL-23 (p19)	HLT2736	Hu	WB, IHC
	MMp19B2	Ms	IF, ELISA Capture
IL-33	BL35172	Hu	WB
	Poly5163	Hu	ELISA Capture
	Poly5165	Ms, Rat	ELISA Capture
IFN-γ	4S.B3	Hu, NHP	WB, ICFC, ELISA
	AN-18	Ms	IP, ELISA Capture, ELISPOT
	B27	Hu, NHP	WB, IHC, ICFC, IP, ELISA
	DB-1	Ms, Rat	WB, IHC, ICFC, ELISA Capture
	H22	Ms	WB, IF, IP, ELISA
	MD-1	Hu, NHP	WB, IHC, ICFC, ELISA Capture
	NIB42	Hu	ELISA Capture
	R4-6A2	Ms	ELISA & ELISPOT Detection
	XMG1.2	Ms	ICFC
TNF-α	6B8	Ms	ELISA Capture
	MAb1	Hu	WB, ELISA Capture, Neut
	MAb11	Hu, NHP	WB, IHC, ICC, IF, ICFC, FC, ELISA, CyTOF®, Neut
	MP6-XT22	Ms	WB, IHC, IF, ICFC, ELISA, CyTOF®
	TN3-19.12	Ms, Rat, Rb	WB, IP, ELISA Capture
	TNF 104C	Hu	WB, FC, FA, ELISA, Neut

†Additional cytokines available



Cytokine Receptor Antibodies†

Specificity	Clone	Reactivity	Application (s)
IL-1R (CD121a)	JAMA-147	Ms	IP, FC
IL-1RA	JK1RA-1	Hu	ELISA Capture
IL-6Rα (CD126)	UV4	Hu	FC
IL-10R (CD210)	1B1.3a	Ms	FC
	3F9	Hu, NHP	IP, FC
IL-17AR (CD217)	BG/hIL17AR	Hu	FC
	W15177A	Hu	FC
IL-18Rα (CD218a)	BG/IL18RA	Ms	FC
	H44	hu	IHC, FC
IL-23R	12B2B64	Ms	FC
IL-33Rα (IL1RL1, ST2)	DIH9	Ms	FC
IFNAR-1 (CD119)	2E2	Ms	WB, IP, FC
	MAR1-5A3	Ms	WB, IP, FC, ELISA
TNF-RI (CD120a)	55R-170	Ms	IP, FC, ELISA Detection
	55R-286	Ms	WB, IP, FC, ELISA Capture
	W15099A	Hu	FC
TNF-RII (CD12b)	3G7A02	Hu	FC
	TR75-32.4	Ms	IP, FC, ELISA

Chemokine Antibodies†

Specificity	Clone	Reactivity	Application (s)
CCL2 (MCP-1)	2H5	Hu, Ms, Rat, NHP	WB, IHC, ELISA Capture
	4E2/MCP	Ms	ELISA & ELISPOT Detection
	5D3-F7	Hu, NHP	WB, IHC, ICFC, IP, ELISA Capture, ELISPOT Detection
CCL5 (RANTES)	J047C5	Hu	ELISA Capture
	VL1	Hu, NHP	WB, IHC, ELISA
CCL11 (Eotaxin)	16D10A40	Hu	WB
	L402H11	Ms	WB
	L403H11	Ms	ELISA Capture
CCL17 (TARC)	Poly5230	Hu	ELISA Detection
CX3CL1	L393H11	Hu	WB
CXCL9 (MIG)	MIG-2F5.5	Ms	IP, ICFC
CXCL10 (IP-10)	J034D6	Hu, NHP	WB, ICFC
	J036G3	Hu	WB, ELISA Capture
	Poly5194	Hu	WB, ELISA Detection
CXCL12 (SDF-1β)	M4201G03	Ms	WB, ELISA Detection
	M4201G11	Ms	IP, ELISA
	W15149A	Hu, Ms	WB
IL-8	BH0814	Hu	ELISA Capture
	E8N1	Hu	ELISA
	H8A5	Hu	ELISA Capture

Chemokine Receptor Antibodies†

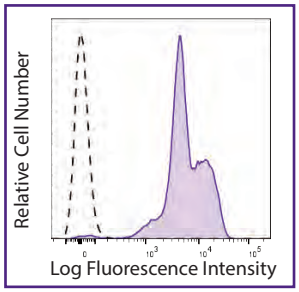
Specificity	Clone	Reactivity	Application (s)
CCR2 (CD192)	K036C2	Hu	FC
	SA203G11	Ms	FC
CX3CR1	2A9-1	Hu, Ms	FC
	8E10.D9	Hu	WB, IHC
CXCR2 (CD182)	5E8/CXCR2	Hu	FC
	SA044G4	Ms	FC
	SA045E1	Ms	FC
CXCR3 (CD183)	CXCR3-173	Ms	FC
	G025H7	Hu, NHP	FC
CXCR4 (CD184)	12G5	Hu, NHP	IHC, ICC, IF, FC, CyTOF®
	L276F12	Ms	FC
CXCR7	10D1-J16	Hu	FC
	8F11-M16	Hu, Ms	FC, ICFC

†Additional cytokine, chemokines, and receptors available

The Blood-Brain Barrier

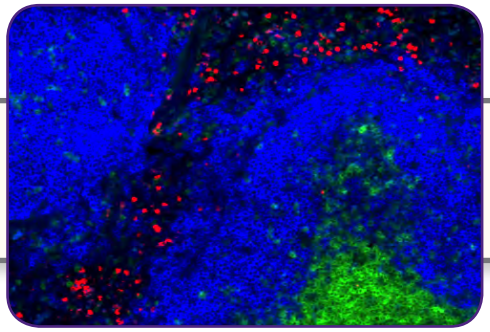
The migration and infiltration of leukocytes from the periphery to the CNS parenchyma under disease conditions is associated with the breakdown of the BBB, which is composed of endothelial cells, surrounded by astroglial basement membranes, further covered by astrocytic endfeet to provide support to endothelial function. Inflammation-induced disturbances in the BBB are partly due to activation of endothelial cells and are characterized by increased expression of: 1) cell adhesion molecules such as ICAM-1 and VCAM-1; 2) pro-inflammatory chemokines such as CCL2/MCP-1 and CXCL10/IP-10; and 3) cytokine receptors such as TNFR and IL-17R. These factors affect the endothelial cell phenotype, and support extravasation and accumulation of infiltrating leukocytes (*e.g.* Th1 and Th17 effector T cells) in the perivascular space. To further gain access into the CNS, these cells secrete matrix metalloproteinases (MMPs) which help breakdown the astrocytic endfeet and the parenchymal basement membrane, and enter the parenchyma where they subsequently contribute to disease progression.

CD18/Integrin β2



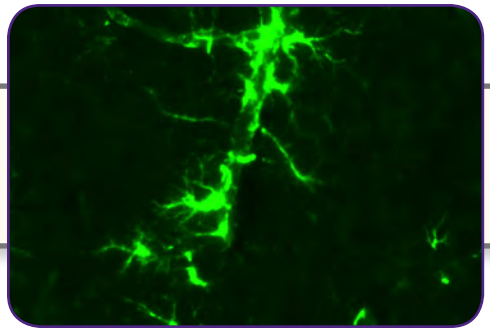
Human peripheral blood lymphocytes stained with PE/Cy7 anti-human CD18 antibody (clone 1B4/CD18, filled histogram) or PE/Cy7 mouse IgG2a, κ PE/Cy7 isotype control (open histogram).

CD18/Integrin β2



Mouse frozen spleen section stained with Alexa Fluor® 594 anti-mouse CD18 (clone M18/2, red), Alexa Fluor® 647 anti-mouse CD3 (clone 145-2C11, green), and Alexa Fluor® 488 anti-mouse/human B220 (clone RA3-6B2, blue) antibodies.

GFAP



FFPE mouse brain tissue stained with anti-GFAP antibody (clone SMI 25).

Cell Adhesion Molecule & Gap Junction Antibodies

	Specificity	Clone	Reactivity	Application (s)
Cell Adhesion Molecules	CD18 (Integrin β2)	1B4/CD18	Hu	FC
		C71/16	Ms	FC
		CBR LFA-1/2	Hu	FC
		M18/2	Ms	IHC, IF, FC
		TS1/18	Hu, Swine	FC
	CD29 (Integrin β1)	P5D2	Hu	FC, Block
	CD49b (Integrin α2)	P1E6	Hu	IHC
	CD49c (Integrin α3)	P1B5	Hu	IHC, IF, IP
	CD49d (Integrin α4)	9C19 (MFR4.B)	Ms	IHC, FC
		9F10	Hu, NHP	IHC, FC
		P4C2	Hu	IF, IP, FC
	CD49e (Integrin α5)	P1D6	Hu	FC
	CD51 (Integrin αvβ5)	P1F6	Hu, Rat, Hamster	FC
	CD54 (ICAM-1)	HA58	Hu	IHC, IF, FC
		HCD54	Hu, NHP	IF, FC
		YN1/1.7.4	Ms	WB, IHC, IP, FC
	CD106 (VCAM-1)	429 (MVCAM.A)	Ms	IHC, IP, FC
		A16047A	Hu	WB
		MR106	Rat	FC
		P3C4	Hu	IHC, IF, IP, FC
		STA	Hu	IHC, IP, FC, ELISA
	CD325 (N-Cadherin)	13A9	Hu, Ms, Rat	WB, IHC, IF, IP
		8C11	Hu	WB, IF, FC
	LPAM-1 (Integrin α4β7)	DATK32	Ms	FC
	Podoplanin (Lymphatic Endothelial Marker)	8.1.1	Ms	IHC, FC
		D2-40	Hu	WB, IHC, IF, ELISA Capture
		NC-08	Hu	IF, FC
Gap Junction proteins	β-Dystroglycan	4F7	Hu, Ms	WB, IHC, IP
	Connexin 43	P1E11	Ms, Rat	WB
		P2C4	Hu, Ms	WB, IHC

Immunoassays for Neuroinflammation Research

Immune cells secrete a variety of cytokines and chemokines in response to inflammatory challenges. In order to quantify these molecules, BioLegend offers a wide range of immunoassay platforms for detection of single and multiple analytes. Our LEGEND MAX™ ELISA Kits, ELISA MAX™ Deluxe and ELISA MAX ™ Standard sets provide a large selection of validated markers that are easy-to-use and offered at an economical price. Our LEGENDplex™ Multi-Analyte Flow Assay Kits are bead-based immunoassays that allow simultaneous quantification of multiple analytes in a single sample using a standard flow cytometer. These kits are available as pre-defined panels or with our Mix and Match System, and offer great flexibility and affordability for users.

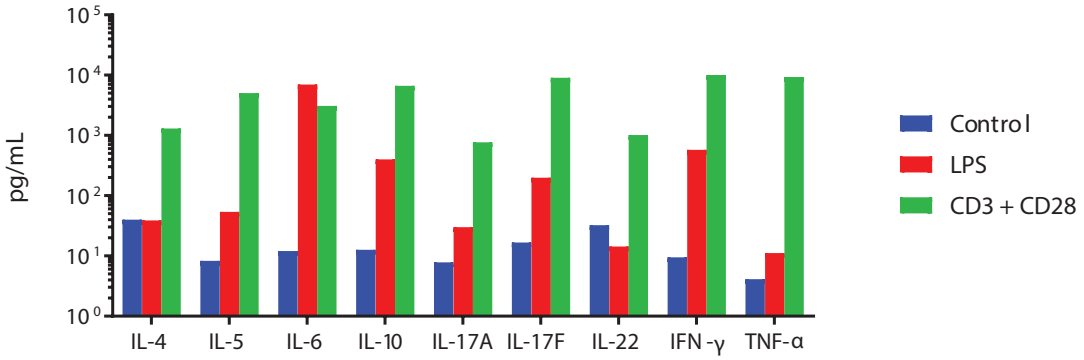
To learn more about BioLegend's immunoassays, visit:
biolegend.com/elisa & biolegend.com/legendplex

Overview of BioLegend's Immunoassay Platforms

	LEGEND MAX™ ELISA Kits	ELISA MAX™ Deluxe Sets	ELISA MAX™ Standard Sets	LEGENDplex™ Assays
Suggested Application	Single Analyte Quantification	Single Analyte Quantification	Single Analyte Quantification	Multi-Analyte Quantification
Format	96-well plate	Flexible	Flexible	Bead
Sample Volume	50 µL	100 µL	100 µL	25 µL
Analytes	1	1	1	Up to 13
Species Reactivity	Hu, Ms, Rat	Hu, Ms, Rat	Hu, Ms	Hu, Ms, Rat, NHP
Features	Pre-coated Plates and All Necessary Reagents to Perform the Assay	Uncoated Plates and All Necessary Reagents Except Wash Buffer and Stop Solution	Pre-titrated Capture and Detection Antibodies, Recombinant Standards, Avidin-HRP	Choice of Plate Format and All Necessary Reagents to Perform the Assay
Assay Time	4 Hours	Overnight (+ 6 Hours)	Overnight (+ 6 Hours)	6 Hours
Required Equipment	Microplate Reader	Microplate Reader	Microplate Reader	Flow Cytometer Capable of Detecting both PE and APC Emission Spectra; Can also use PE and PerCP or PerCP/Cy5.5 channels
	Plate Shaker	Plate Shaker	Plate Shaker	Plate Shaker
	Log-Log Graph Paper or Curve Fitting Software	Log-Log Graph Paper or Curve Fitting Software	Log-Log Graph Paper or Curve Fitting Software	Data Analysis Software (Free with Kit Purchase)
				Vacuum Filtration Unit (for Filter Plates) or Centrifuge with Swinging Adaptor (For Microplates)

LEGENDplex™ Product Highlight

Human T Helper Cytokine Panel



Human PBMCs (1 x 10^6 cells/ml) were cultured under various conditions (LPS, 100 ng/mL; CD3, 1 µg/mL plate-coated; CD28, 1 µg/mL soluble). Supernatants were collected after 48 hours and assayed with the LEGENDplex™ Human Th Cytokine Panel.

MojoSort™ Magnetic Cell Separation System

BioLegend's MojoSort™ is a magnetic bead-based cell separation system designed to isolate and purify cells from heterogeneous populations. It is compatible with multiple magnetic separation platforms, and the cells can be isolated by positive or negative selection. In positive selection, the cells of interest are isolated using antibody-conjugated magnetic nanobeads. In negative selection, the population of interest is untouched and all other cell types are labeled with the magnetic nanoparticles, and then depleted from the sample. MojoSort™ offers a fast and easy solution to isolate pure and functional cells at an outstanding value.

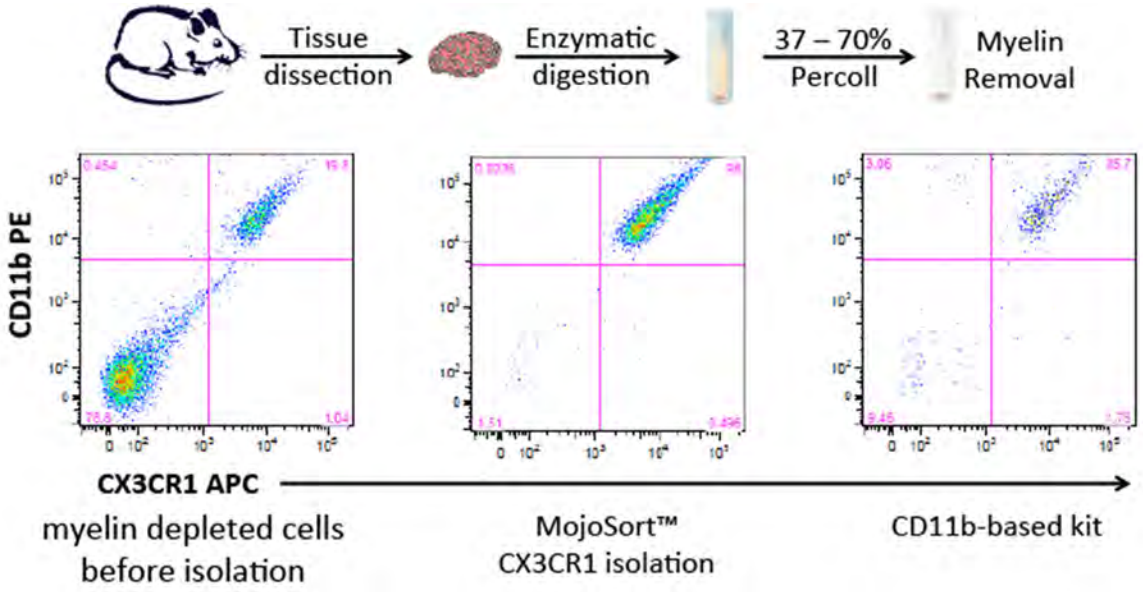
Learn more about MojoSort™ at: biolegend.com/mojosort

MojoSort™ Products

Nanobeads	Selection Kits	Isolation Kits	Ancillary Products
Human CD4 Nanobeads	Human CD14 Selection Kit	Human CD14+ Monocyte Isolation Kit	MojoSort™ Buffer (5X)
Human CD45 Nanobeads	Human CD4 T Cell Selection Kit	Human CD4 T Cell Isolation Kit	MojoSort™ Magnet 5 mL
Mouse CD4 Nanobeads	Mouse CX3CR1 Selection Kit	Human CD4 Naïve T cell Isolation Kit	MojoSort™ Magnet 14 mL
Mouse CD11c Nanobeads		Mouse CD4 T Cell Isolation Kit	
Mouse CD45 Nanobeads		Mouse CD4 Naïve T cell Isolation Kit	

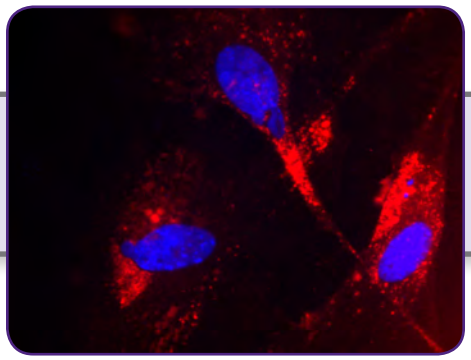
MojoSort™ Product Highlight

MojoSort™ Mouse CX3CR1 Selection Kit



Isolation of CX3CR1 positive Microglia from neonatal mice
A single cell suspension from C57BL/6 mouse brain was prepared using Trypsin digestion and 70/37/30% percoll gradient to isolate CX3CR1+ microglia using the MojoSort™ Mouse CX3CR1 Selection Kit. Cells were gated on CD11b and CX3CR1. Left plot shows cells after myelin removal and before magnetic sorting, middle plot shows cells after isolation with MojoSort™ Mouse CX3CR1 Selection Kit, right plot shows results obtained using a standard CD11b Isolation kit. Debris and dead cells were gated out with 7AAD viability dye.

Isolated CX3CR1 Microglia Adhere to Glass



Positively isolated CX3CR1 cells were cultured for 12 days. Then the cells were stained with CD11b (red) and DAPI (blue). The image was captured by using 40x objective.

Recombinant Proteins

BioLegend's growing portfolio of recombinant proteins now contains over 600 functional proteins for human, mouse, and rat, and can be used for many *in vitro* and *in vivo* neuroscience bioassays. Our recombinant proteins include cytokines, chemokines, growth factors, enzymes and regulators, adhesion molecules, and soluble receptors that are expressed with either mammalian, *E. coli*, or insect expression system. Our proteins are over 95% pure, validated in-house to ensure reproducibility, biologically active, and compare favorably against competitors' products.

To learn more, visit: biolegend.com/recombinant_proteins

Recombinant Proteins Product Highlight

Inhibition of neurite outgrowth by recombinant human OMG

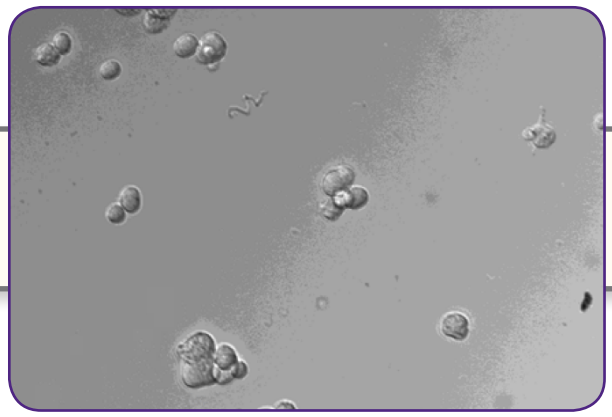


Figure A: Human OMG (Oligodendrocyte-myelin glycoprotein) completely inhibits neurite outgrowth of E13 chick DRG neurons induced by laminin substrate.

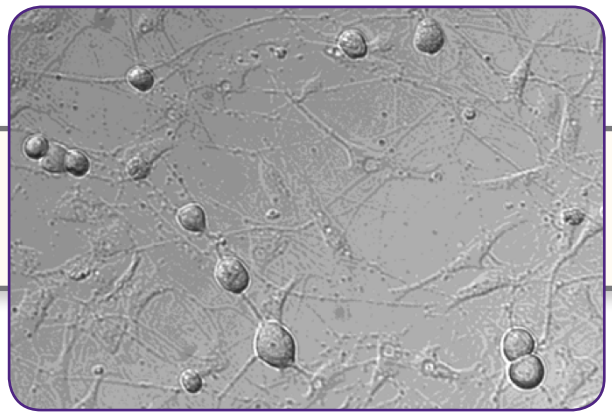
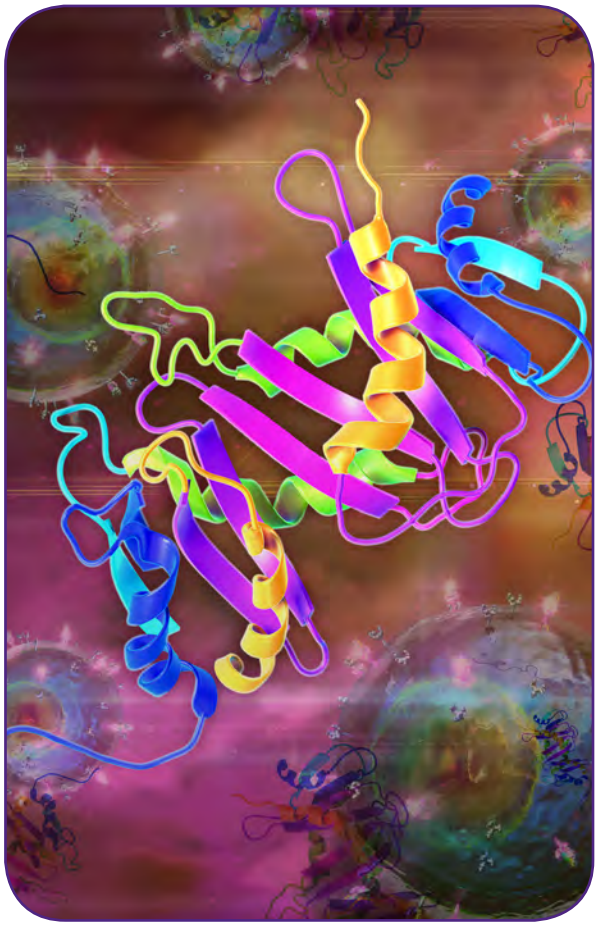


Figure B: Buffer control (PBS) shows no inhibition of neurite outgrowth of E13 chick DRG neurons induced by laminin substrate.



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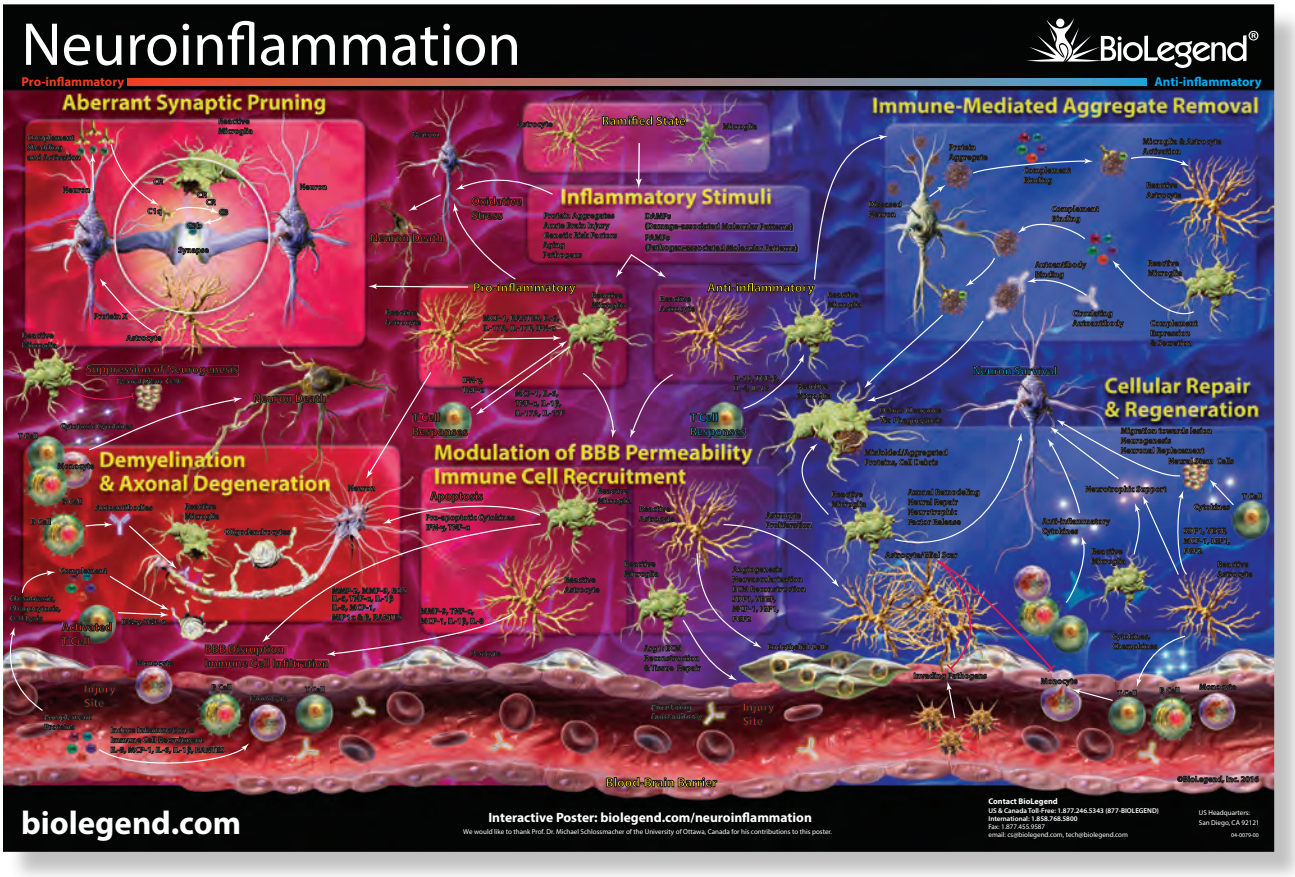

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