Neuroimmune Pharmacology

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Tsuneya Ikezu
Howard E. Gendelman

Preface

In the past two decades, enormous strides have been made in our understanding of the relationships between inflammation, innate immune responses, adaptive immune responses, and degenerative human diseases. The developing information has mostly appeared in specialty journals that have dealt only with isolated aspects of these tightly related fields. As a result, contemporary scientists have had a difficult time finding sources, even in review articles, that provide an integrated picture. This volume, by assembling chapters that demonstrate the relationship between these historically separated fields, overcomes that difficulty. There are sections on immunology of the nervous system, diseases that result from immunological dysfunction, current therapeutic approaches, and prospects for the future. Overall, it integrates cutting-edge neuroscience, immunology, pharmacology, neurogenetics, neurogenesis, gene therapy, adjuvant therapy, proteomics, and magnetic resonance imaging. It is a rich harvest and readers will gain a perspective that has not previously been so readily available. Exposure to such a wealth of ideas is bound to inspire readers to undertake new and productive research initiatives.

The modern era of research into neuroinflammation and its relationship to neurodegenerative diseases began in the 1960's with the elaboration by Ralph van Furth of the monocyte phagocytic system. He injected labeled monocytes into animals and followed their migration and maturation into resident phagocytes in all body tissues. This provided closure between Metchnikoff's 1882 discovery of mesodermal attack cells in starfish larvae, which he named phagocytes, and del Rio Hortega's 1919 discovery of phagocytic mesodermal cells entering the brain, which he named microglia. Hortega's results had always been questioned and for more than two decades the controversy continued as to whether microglia were truly phagocytes of mesodermal origin or were merely typical brain cells of epidermal origin. Were they truly the effector cells in brain inflammation or were they merely housekeeping cells with an as yet undefined role? Resolving the controversy required development of the techniques of immunohistochemistry and monoclonal antibody production.

These tools for exploring brain biochemistry at the cellular level opened new vistas for understanding brain functioning and the pathogenesis of human disease. Using these tools, our laboratory and that of Joseph Rogers in Sun City demonstrated that HLA-DR was strongly expressed on activated microglia. The identification of HLA-DR, a well-known leukocyte marker displayed by antigen presenting cells, on these cells vindicated both Hortega and van Furth. The way was paved for many productive investigations exploring the properties of microglial cells and their relationship to inflammation and immune responses. This example of a conjunction between a fundamental concept and technical advances to establish its validity has been repeated many times since, as the chapters in this volume illustrate.

For a time, the concept that the brain is immunologically privileged held sway amongst neuroscientists. This was based on a narrow view that only the invasion of brain by lymphocytes could be taken as evidence of an inflammatory response. Since lymphocytes and antibodies are relatively restricted in their ability to cross the blood brain barrier, the brain was supposedly isolated from self-attack. But immunochemistry, coupled with newly developed molecular biological techniques, revealed that a spectrum of inflammatory mediators, including many known to cause tissue damage, were produced within the brain by resident brain cells. These discoveries required entirely new interpretations as to the nature of neuroinflammation and its relationship to immune responses. The innate immune system, operating at the local level in the brain, has clearly proved to be the first line of defense. Indeed, the basic discoveries from studying the response of brain in a variety of neurological diseases, is causing a reevaluation of a number of peripheral degenerative disorders where innate immune responses, which had previously been ignored, have been shown to play a critical role in their pathogenesis. In other words, those studying the brain are providing immunologists with revolutionary new concepts regarding classical peripheral diseases. The insights of Part 1 of this volume need to be interpreted in this broader context.

Part 2 moves from the general to the specific. Individual neurological disorders and details of their pathogenesis are presented. They involve disorders where innate immune responses predominate, as in Alzheimer's disease, to others such as multiple sclerosis, where adaptive immune responses predominate, and still others, which seem to involve both. We have suggested that diseases involving self-damage generated by innate immune responses be defined as autotoxic to differentiate them from classical autoimmune diseases where self damage is generated by adaptive immune responses. The common theme, however, is the involvement of microglia as the effector cells.

Part 2 also deals with neurogenetics. No field of neuroscience is moving so rapidly. The methodology for linking familial disease to DNA mutations commenced in the late 70's through identification of restriction fragment linked polymorphisms. By 1983, when James Gusella and his colleagues demonstrated a linkage of the G8 fragment to Huntington disease only about 18 markers were known. Now over 500,000 single nucleotide polymorphisms have been localized so that every centimorgan of the human genome can be explored. This advance has been coupled with rapid methods for sequencing DNA. The section on Genetics must be

regarded as the tiny tip of a giant iceberg where much below the surface will soon be revealed.

The ultimate objective of neuroscientists studying human disease is to find more effective treatments. Part 3 covers the pharmacology of existing drugs, as well as describing approaches now in clinical evaluation, and those still at the bench level. Some of these include concepts that depart from established therapeutic approaches giving the reader much food for thought.

To complete the picture, there is a final chapter on imaging of the brain. The brain is inaccessible, and imaging provides a view of how it functions in vivo and how it is affected by neurological disease. Most importantly, it now provides methods for objectively measuring the effects of therapeutic agents in diseases where progressive brain degeneration occurs.

In summary, this is a volume not to be put on the shelf as a reference text, but to be read cover to cover by aspiring neuroscientists.

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Abbreviations

Neuroimmune Pharmacology Abbreviations

¹ H	proton	AHSCT	autologous hematopoietic stem cell transplantation
¹ H-MRSI	proton magnetic resonance spectroscopic imaging	AICA	anterior inferior cerebellar artery
2D SDS-PAGE	two-dimensional polyacrylamide gel electrophoresis	AID	activation-induced (cytidine) deaminase
3'UTR	3'-untranslated region	AIDP	acute inflammatory demyelinating polyradiculoneuropathy
3HK	3-hydroxykynurenine	AIDS	acquired immunodeficiency syndrome
5-ASA	5-aminosalicylic acid	AIF	apoptosis inducing factor
5-HIAA	5-hydroxyindole acetic acid	AIRE	autoimmune regulator
5-HT	5-hydroxy tryptophan	AIS	anterior chamber associated immune deviation (ACAID)-inducing signal
5-HT	5-hydroxytryptamine	ALS	amyotrophic lateral sclerosis
6-OHDA	6-hydroxydopamine	AMAN	acute motor axonal neuropathy
8-OHdG	8-hydroxy-2'-deoxyguanosine	AMN	adrenomyeloneuropathy
γc	common γ-chain	AMPA	α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid
AAV	adeno-associated virus	AMSAN	acute motor-sensory axonal neuropathy
Ab	antibody	ANS	autonomic nervous system
Aβ	amyloid-β	AP-1	activating protein-1
ABP	actin-binding protein	APAF 1	apoptotic peptidase activating factor 1
AC	anterior chamber	APC	antigen presenting cells
ACAID	anterior chamber associated immune deviation	aPKC	atypical protein kinase C
αCamKII	α-calcium/calmodulin-dependent protein kinase II	aPL	antiphospholipid antibody
ACh	acetylcholine	APO1	apoptosis antigen 1 (Fas/CD95)
AChE	acetylcholinesterase	apoE	apolipoprotein E
ACTH	adrenocorticotrophic hormone (pro-opiomelanocortin; POMC)	APP	β-amyloid precursor protein
AD	Alzheimer's disease	APPs	acute phase proteins
ADAM	a disintegrin and metalloprotease	ARE	AU-rich response element
ADCC	antibody-dependent cellular cytotoxicity	ARMD	age-related macular degeneration
ADEM	acute disseminated encephalomyelitis	ART	antiretroviral therapy
AF	activation factor	ASL	arterial spin-labeled
Ag	antigens	ASTIN	acute stroke therapy by inhibition of neutrophils
AGE	advanced glycation endproducts	AT	adoptive transfer
AGM	aorta-gonad mesonephros	ATL	adult T cell leukemia
		AVP	arginine vasopressin
		AZT	3'-azidothymidine/zidovudine

BACE	beta-site amyloid precursor protein cleaving enzyme	CJD	Creutzfeldt-Jakob disease
BBB	blood-brain barrier	CLA	cutaneous leukocyte antigen
BCR	B-cell receptor	CLP	common lymphoid progenitor
BCRP	breast cancer resistance protein	CMAF	compound motor action potential
BDNF	brain-derived neurotrophic factor	CMC	critical micelle concentration
bFGF	basic fibroblast growth factor (FGF2)	CMP	common myeloid precursor
bHLH	basic helix-loop-helix	CMT	Charcot-Marie-Tooth (disease)
BHV-1	bovine herpesvirus-1	CMV	cytomegalovirus
BLIMP-1	B lymphocyte-induced maturation protein-1	CNG	cGMP-gated
BLV	bovine leukemia virus	CNPase	cyclic nucleotide 3' phosphohydrolase
BM	bone marrow	CNS	central nervous system
BMP	bone morphogenetic protein	CNTF	ciliary neurotrophic factor
BMVEC	brain microvascular endothelial cell	CO	cytochrome oxidase
BrdU	bromodeoxyuridine	COMT	catechol-O-methyltransferase
BRM's	biological response modifiers	Con A	concanavalin A
BSE	bovine spongiform encephalopathy	COP-1	copolymer-1
BTLA	B and T lymphocyte attenuator	COX	cyclooxygenase (prostaglandin-endoperoxide synthase; PTGS)
C/EBP	CCAAT box/ enhancer binding protein	CR	complement receptor
C3d	complement C3 fragment d	CRaBP	cellular retinal binding protein (retinaldehyde binding protein 1; RLBP1)
C4d	complement C4 fragment d	CRE	cAMP-responsive element
CA	cornu ammonis	Cre	creatine
CaMKII	calcium/calmodulin-dependent protein kinase II	CREB	cAMP-response element binding protein
CAMs	cell adhesion molecules	CRH	corticotrophin-releasing hormone
CARD15	NOD2/caspase recruitment domain 15	CRP	C-reactive protein
CB	cannabinoid	CRVO	central retinal vein occlusion
CB1	cannabinoid receptor 1	CSF	cerebrospinal fluid
CB2	cannabinoid receptor 2	CSF-1R	colony stimulating factor receptor
CBA	cytokine bead arrays	CSPG	chondroitin sulfate proteoglycans
CBF	cerebral blood flow	CT	computed tomography
CBF1	C promoter binding factor 1	CTA	computed tomographic angiography
CBP	cAMP-response element binding protein (CREB)-binding protein	cTEC	cortical thymic epithelial cell (TEC)
CBV	cerebral blood volume	CTL	cytotoxic T lymphocyte
CCT	central corneal thickness	CTLA-4	cytotoxic T lymphocyte antigen-4
CD	cluster of differentiation	CVO	circumventricular organ
CD11b	complement component 3 receptor 3 subunit (integrin alpha M; ITGAM)	Cx	connexin
CD40L	CD40 ligand (TNFSF5)	cyto c	cytochrome c
CDR	complementarity-determining region	D1R	type-1 family of dopamine receptors
CDV	canine distemper virus	D ⁹ -THC	D ⁹ -tetrahydrocannabinol
CFT	2-β-carbomethoxy-3β-(4-fluorophenyl) tropane	DA	Daniel's strain of Theiler's virus
cGMP	cyclic guanosine 5'-monophosphate	DA	dopamine
CGRP	calcitonin-gene related peptide	DAF	decay-accelerating factor
CHAT	choline acetyltransferase	DAG	diacylglycerol
CHN	congenital hypomyelinating neuropathy	DAT	dopamine transporter (solute carrier family 6A3; SLC6A3)
Cho	choline	DβH	dopamine-β-hydroxylase
CIDP	chronic inflammatory demyelinating polyradiculoneuropathy	DC	dendritic cells
CINC1	cytokine-induced neutrophil chemoattractant-1	DCX	doublecortin
		ddC	dideoxycytidine
		ddI	dideoxyinosine
		DG	dentate gyrus
		dGTP	deoxyguanosine triphosphate

DHA	docosahexaenoic acid	FDOPA	6-[(18)F]fluoro-L-dopa
Dhh	desert hedgehog	FFI	fatal familial insomnia
DIGE	Difference Gel Electrophoresis	FGF	fibroblast growth factor
DISC	death-inducing signaling complex	FID	free induction decay
DN	double/dominant negative	FIV	feline immunodeficiency virus
Doc2	double C2 protein	FKN	fractalkine (CX3CL1)
DOR	delta-opioid receptor	fMRI	functional magnetic resonance imaging
Dox	doxorubicin	Foxp3	forkhead box P3 transcription factor
Dox	doxycycline	FRC	fibroblastic reticular cell
DRPLA	dentatorubral-pallidoluysian atrophy	FRS2	fibroblast growth factor receptor substrate 2
DSI	depolarization induced suppression of inhibition	FS	Fisher syndrome
DSPN	distal sensory peripheral neuropathy	FTD	frontotemporal dementia
DSS	Dejerine-Sottas syndrome	FT-ICR	fourier transformed ion cyclotron resonance mass spectrometry
DTH	delayed-type hypersensitivity	Fz/PCP	Ffizzled/planar cell polarity
DTI	diffusion tensor imaging	GA	glatiramer acetate
DWI	diffusion weighted imaging	GABA	gamma-aminobutyric acid
E2F	early-region-2 transcription factor	GAD	glutamate decarboxylase
EAE	experimental allergic/autoimmune encephalomyelitis	GalC	galactocerebroside
EAN	experimental allergic/autoimmune neuritis	GALT	gut-associated lymphoid tissue
EAU	experimental autoimmune uveitis	GAP	GTPase activating protein
EBV	Epstein-Barr virus	GAPDH	glyceraldehyde 3 phosphate dehydrogenase
ECT	electroconvulsive therapy	GBM	glioblastoma multiforme
EDSS	expanded disability status scale	GBS	Guillain-Barré syndrome
EEG	electroencephalography	GC	germinal center
EGC	embryonic germ cell	GCDC	germinal center dendritic cell
EGF	epidermal growth factor	GCL	ganglion cell layer
EGFR	epidermal growth factor receptor	GL	granular cell layer
ELAVL4	embryonic lethal, abnormal vision, Drosophila-like 4	GC-MS	gas chromatography combined with mass spectrometry
eLTP	early long-term potentiation	G-CSF	granulocyte-colony stimulating factor
EMG	electromyography	Gd	gadolinium
EndoG	endonuclease G	GDF	growth and differentiation factor
EOAD	early-onset Alzheimer's disease	GDNF	glial-derived neurotrophic factor
EPI	echo-planar imaging	GEF	GDP-GTP exchange factor
EPSP	excitatory postsynaptic potential	GFAP	glial fibrillary acidic protein
ER	endoplasmic reticulum	GFP	green fluorescent protein
ERK2	extracellular signal-regulated kinase 2	GKAP	guanylate kinase-associated protein
ESC	embryonic stem cell	GLC1A	chromosome 1 open-angle glaucoma gene
ESI-MS/MS	electrospray ionization-mass spectrometry/mass spectrometry	Gln	glutamine
ET	endothelin	GM-CSF	granulocyte macrophage-colony stimulating factor
ETP	early T lineage progenitor	GMP	granulocyte monocyte precursor
FA	fractional anisotropy	GnRH	gonadotropin-releasing hormone
FAD	familial Alzheimer's disease	GPCR	G-protein-coupled receptor
fALS	familial amyotrophic lateral sclerosis	GPI	glycosylphosphatidylinositol
FasL	Fas ligand (FASLG)	GR	glucocorticoid receptor
FcγR-1	Fc receptor, IgG, high affinity-1	GRIP	glucocorticoid receptor-interacting protein
fCJD	familial Creutzfeldt-Jakob disease	GRO-α	growth-related oncogene alpha
FcR	Fc receptor	GSH	glutathione
FDC	follicular dendritic cell		
FDG	fluorodeoxyglucose		

GSS	Gerstmann-Straussler-Scheinker disease	IGF	insulin-like growth factor
GSTO1	glutathione s-transferase omega-1	IgG	immunoglobulin G
G ^T	G-protein transducin	IGIV	Immunoglobulin intravenous therapy
GUCY	guanylate cyclase	lhh	Indian hedgehog
HAD	HIV-associated dementia	IIDD	idiopathic inflammatory demyelinating disease
HAM/TSP	HTLV-I associated myelopathy/tropical spastic paraparesis	IκB	inhibitory kappa B
HAT	histone acetyltransferase	IKK	IκB kinase
HBsAg	hepatitis B surface antigen	IL	interleukin
HCMV	human cytomegalovirus	IL1RA	IL-1 receptor antagonist
HD	Huntington's disease	ILBD	incidental Lewy body disease
HDAC	histone deacetylase	ILM	inner limiting membrane
HES	hairly and enhancer of split homolog	IM	intramuscular
HEV	high endothelial venule	IMPDH	inosine monophosphate dehydrogenase
HFS	high frequency stimulation	iNKR	inhibitory natural killer cell receptor
Hh	hedgehog	INL	inner nuclear layer
HHH	hypervolemic-hemodilution and hypertensive	iNOS	inducible nitric oxide synthase (NOS2A)
HHV-6	human herpes virus-6	IOP	intraocular pressure
HIV-1	human immunodeficiency virus type 1	IP	interferon-inducible protein
HIVE	human immunodeficiency virus encephalitis	InsP3R	inositol 1,4,5-triphosphate receptor
HLA	human leukocyte antigen	IPL	inner plexiform layer
HLH	helix-loop-helix	IRAK	IL-1 receptor associated protein kinase
HMG-CoA	3-hydroxy-3-methylglutaryl coenzyme A	IRBP	interphotoreceptor retinoid-binding protein
HNE	4-Hydroxy-2-nonenal	IRF	interferon regulatory factor
hnRNP-A1	heterogeneous nuclear ribonuclear protein-A1	ISCOM	immunostimulating complexes
HPA	hypothalamic-pituitary-adrenal	ISH	in situ hybridization
HSC	hematopoietic stem cell	IT15	interesting transcript 15
Hsp	heat-shock protein	ITAM	immunoreceptor tyrosine-based activation motif
HSV	herpes simplex virus	ITGAM	integrin, alpha M
HSVE	herpes simplex virus-mediated encephalitis	ITR	inverted terminal repeat
HTLV	human T-cell lymphotropic virus type	IVDU	intravenous drug use
HTRA2	high temperature requirement serine protease 2	IVIg	intravenous immunoglobulin
Htt	huntingtin	JAK	Janus kinase
HvEa	herpesvirus entry mediator A	JEV	Japanese encephalitis virus
I-1	regulatory protein inhibitor-1	JNK	c-Jun N-terminal kinase
IBS	inflammatory bowel syndrome	KLH	keyhole limpet hemocyanin
ICAM	intracellular adhesion molecule	KOR	kappa opioid peptide receptor
ICAT	isotope coded affinity tags	KYN	kynurenine
ICH	intracerebral hemorrhage	KYNA	kynurenic acid
iCJD	iatrogenic Creutzfeldt-Jakob disease	LAK	lymphokine-activated killer (cell)
ICOS	inducible co-stimulatory molecule	L-AP4	L-2-amino-4-phosphonobutyric acid
Id	inhibitor of differentiation	LAT	latency associated transcript
IDE	insulin degrading enzyme	LB	Lewy bodies
IDO	indoleamine 2,3-dioxygenase	LC	locus coeruleus
IE	immediate early	LCA	leukocyte common antigen
IF	intermediate filament	LC-FTICR MS	liquid chromatography fourier transform
IFN	interferon	LC-MS	ion cyclotron resonance mass
Ig	immunoglobulin		liquid chromatography combined with mass spectrometry

LC-UV-SPE-NMR	liquid chromatography, UV detection, solid phase extraction, and nuclear	MHV	mouse hepatitis virus
LD	linkage disequilibrium	mI	myoinositol
LDL	low density lipoprotein	MIF	migration inhibitory factor
LFA-1	leukocyte function-associated antigen-1 (integrin beta 2; ITGB2)	Mint1	Munc-18 interacting protein 1
LGN	lateral geniculate nucleus	MIP	macrophage inflammatory protein
LIF	leukemia inhibitory factor	MJO	Machado-Joseph disease
Lingo-1	Leucine-rich-repeat and Ig domain containing Nogo-receptor interacting protein-1	MME	membrane metallo-endopeptidase (neprilysin)
LMN	lower motor neuron	MMP	matrix metalloproteinase
LOAD	late-onset Alzheimer's disease	MMSE	Mini-Mental State Examination
LOS	lipooligosaccharide	MNGC	multi-nucleated giant cell
LPA	lysophosphatidic acid	Mn-SOD	manganese superoxide dismutase
LPS	lipopolysaccharide	MOAT	multi-specific organic anion transporter
LRR	leucine-rich repeat	MOBP	myelin associated/oligodendrocyte basic protein
LRRK2	leucine-rich repeat kinase 2	MOG	myelin oligodendrocyte glycoprotein
LT	lymphotoxins	MOI	multiplicity of infection
LTD	long-term depression	MOR	mu opioid receptor
LTP	long-term potentiation	MOSP	myelin/oligodendrocyte specific protein
LTR	long-terminal repeat	MP	mononuclear phagocytes
LT-βR	lymphotoxin beta receptor	MPA	mycophenolic acid
MAC	membrane attack complex	MPL	monophosphoryl lipid A
MAdCAM-1	mucosal addressin cell adhesion molecule-1	MPO	myeloperoxidase
MAG	myelin associated glycoprotein	MPP ⁺	1-methyl-4-phenylperydinium
MAML	mammalian mastermind-like	MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
MAO	monoamino-oxidase	MR	mineralocorticoid receptors
MAP	microtubule-associated protein	MRA	magnetic resonance angiography
MAPK	mitogen-activated protein kinases	MRI	magnetic resonance imaging
Mash1	mammalian achaete-scute homologue 1	MRP	multidrug resistance protein
MBGI	myelin-based growth inhibitor	MRS	magnetic resonance spectroscopy
MBP	myelin basic protein	MRSI	magnetic resonance spectroscopic imaging
MC-1R	melanocortin-1 receptor	MS	multiple sclerosis
MCMD	minor cognitive motor disorder	MSA	multisystem atrophy
MCP	membrane cofactor protein (CD46)	MSCs	myelinating Schwann cells
MCP-1	monocyte chemoattractant protein-1 (CCL2)	MSN	medium spiny neuron
M-CSF	macrophage-colony stimulating factor (CSF1)	mSOD1	mutant Cu ²⁺ /Zn ²⁺ superoxide dismutase 1
MD	major depression	MSRV	multiple sclerosis retrovirus
MDD	major depressive disorder	MT	magnetization transfer
MDM	monocyte-derived macrophages	mTEC	medullary thymic epithelial cell
MDP	muramyl-dipeptide	mTOR	mammalian target of rapamycin
MDP	monocytes and dendritic cell progenitor	MTR	magnetization transfer ratio
MDR	multidrug resistant	MUC1	mucin type 1 glycoprotein
MEG	magnetoencephalography	MuLV	murine leukemia virus
MEPP	miniature end-plate potential	Munc-18	mammalian homologue of unc-18
MFS	Miller Fisher syndrome	MVE	Murray Valley encephalitis virus
MHC	major histocompatibility complex	MZ	marginal zone
MHC-II	class II major histocompatibility complex	NAA	N-acetyl-aspartate
MHPG	methoxy-hydroxy-phenylethanolamine glycol	NAC	N-acetyl cysteine
		NADPH	nicotinamide adenine dinucleotide phosphate
		NCAM	neural cell adhesion molecule
		NE	norepinephrine

NET	norepinephrine transporter	OPCA	olivopontocerebellar atrophy
NeuN	neuronal nuclei	OPL	outer plexiform layer
NF	neurofilament	ORF	open reading frame
NF- κ B	nuclear factor- κ -B	ORN	olfactory response neuron
NFAT	nuclear factor of activated T lymphocytes	OSP	oligodendrocyte-specific protein
NFL	nerve fiber layer	OVA	ovalbumin
NFT	neurofibrillary tangles	P ₀	myelin protein zero
Ng-CAM	neuronal-glia cell adhesion molecule (L1/NILE)	p75 ^{NTR}	p75 neurotrophin receptor (nerve growth factor receptor; NGFR)
NGF	nerve growth factor	PACAP	pituitary adenylate cyclase activating polypeptide
NgR	Nogo-66 receptor	PAF	platelet activating factor
NICD	Notch intracellular domain	PAG	periaqueductal gray
NK	natural killer (cells)	PAMP	pathogen-associated molecular pattern
NKT	natural killer T (cells)	PARP	poly(ADP-ribose) polymerase
NMDA	N-methyl-D-aspartate	PASAT	Paced Auditory Serial Addition Test
NMDAR	N-methyl-D-aspartate receptors	PBBS	peripheral benzodiazepine binding sites
NMJ	neuromuscular junction	PBL	peripheral blood lymphocyte
NMO	neuromyelitis optica	PBMC	peripheral blood mononuclear cell
NMR	nuclear magnetic resonance	PBR	peripheral benzodiazepine receptor
NMSCs	nonmyelinating Schwann cells	PCP	phencyclidine
nNOS	neuronal nitric oxide synthase	PD	Parkinson's disease
NNRTIs	nonnucleoside analogue reverse transcriptase inhibitors	PD1	program death-1
NO	nitric oxide	PDGF	platelet-derived growth factor
NOS	nitric oxide synthase	PDTC	pyrrolidine dithiocarbamate
NOT	nucleus of the optic tract	PE	plasma exchange
NPC	neural progenitor cell	PEG	polyethylene glycol
NPY	neuropeptide Y	PEI	polyethyleneimine
NPZ-8	neuropsychological Z score for 8 tests	PENK	proenkephalin
NR	nuclear receptor	PERG	pattern electroretinogram
NRG	neuregulin	PET	positron emission tomography
NRL	nuclear receptor ligand	PG	prostaglandin
NRTI	nucleoside analogue reverse transcriptase inhibitors	Pgp	P-glycoprotein
NSAID	non-steroidal anti-inflammatory drug	PHF	paired helical filament
NSC	neural stem cell	PI	phosphatidylinositol
NSE	neuron specific enolase	PI3K	phosphatidylinositol-3-kinase
NSF	N-ethylmaleimide sensitive factor	PICA	posterior inferior cerebellar artery
NT	3-nitrotyrosine	PICK1	protein interacting with C kinase 1
NTF	neurotrophin	PKA	cAMP-dependent protein kinase
NVU	neurovascular unit	PKG	protein kinase G
OB	olfactory bulb	PLGA	poly(D,L-lactide-coglycolide)
OCB	oligoclonal band	PLP	proteolipid protein
OE	olfactory epithelium	PMCA	plasma membrane bound Ca ²⁺ -ATPase
OHT	ocular hypertension	PMD	Pelizaeus-Merzbacher disease
OL	oligodendrocyte	PMN	polymorphonuclear (leukocyte)
OLM	outer limiting membrane	PMP22	peripheral myelin protein 22
OMgp	oligodendrocyte-myelin glycoprotein	PNS	peripheral nervous system
OMP	olfactory marker protein	POAG	primary open-angle glaucoma
ONH	optic nerve head	polyQ	polyglutamine
ONL	outer nuclear layer	POMC	pro-opiomelanocortin
OP	oligodendrocyte progenitors	POU3F2	POU class 3 homeobox 2
OPC	oligodendrocyte progenitor cell	PP	protein phosphatase
		PPAR	peroxisome proliferator activated receptor

PPF	paired-pulse facilitation	SAPAP	SAP-associated protein (discs, large homolog-associated protein-1; DLGAP1)
PPG	poly(propylene glycol)	SAPK	stress-activated protein kinase (JNK, MAPK8)
PP-MS	primary progressive multiple sclerosis	sAPP	secreted β -amyloid precursor protein
PR	photoreceptor	SBMA	spinobulbar muscular atrophy
PrPc	cellular prion protein	SCs	Schwann cells
PrP ^{Pres}	protease resistance prion	SC	superior colliculus
PrPsc	disease-associated prion protein	SCA-3	spinocerebellar ataxia-3
PRR	pattern recognition receptor	scFv	single chain Fv antibodies
PS	presenilin (PSEN)	SCID	severe combined immunodeficiency
PSA-NCAM	poly-sialylated form of the neural cell adhesion molecule	sCJD	sporadic Creutzfeldt-Jakob disease
PSCs	perisynaptic Schwann cells	SCPs	Schwann cell precursor
PSD	postsynaptic density	sCrry	soluble complement receptor-related protein y
PSP	progressive supranuclear palsy	SDF-1	stromal cell-derived factor 1 (CXCL12)
PSW	periodic sharp wave	SEC	sinus endothelial cell
Ptc	patched, a hedgehog receptor	SELDI-TOF	surface enhanced laser desorption ionization time-of-flight
PTP	post-tetanic potentiation	SER	smooth endoplasmic reticulum
PVL	periventricular leukomalacia	SERCA	sarco(endo)plasmic reticulum Ca ²⁺ -ATPase
PVN	paraventricular nucleus	SERT	serotonin transporter
RA	rheumatoid arthritis	sFI	sporadic fatal insomnia
Rag	recombination-activating gene	SGLPG	sulfated glucuronyl lactosaminyl paragloboside
RAGE	receptor for advanced glycation end product	SGZ	subgranular zone
RANTES	regulated upon activation normal T-cell expressed and secreted (CCL5)	Shh	sonic hedgehog
RAS	renin-angiotensin system	sIg	surface immunoglobulin
Rb	retinoblastoma	sIL-2R	soluble IL-2 receptor
REM	rapid eye movement	SITA	Swedish interactive thresholding algorithm
RER	rough endoplasmic reticulum	SIV	simian immunodeficiency virus
RF	radiofrequency	SLE	systemic lupus erythematosus
RFLPs	restriction fragment length polymorphisms	SMAC	second mitochondrial-derived activator of caspase
RIM	Rab3-interacting molecule	SMase	sphingomyelinase
RIP	receptor interacting protein	SMN	survival motor neuron gene
RMS	rostral migratory stream	SN	substantia nigra
RNAi	RNA interference	SNAP	sensory nerve action potential
RNS	reactive nitrogen species	SNAP-25	synaptosome-associated protein of 25,000 daltons
ROCK	Rho kinase	SNARE	NSF attachment receptor
ROI	reactive oxygen intermediate	SNpc	substantia nigra pars compacta
ROR γ	retinoic-acid-receptor-related orphan receptor- γ	SNPs	single nucleotide polymorphisms
ROS	reactive oxygen species	SNS	sympathetic nervous system
RPE	retinal pigment epithelial (cells)	SOCS	suppressors of cytokine signaling
RR-MS	relapsing and remitting multiple sclerosis	SOD1	superoxide dismutase 1
RTK	receptor tyrosine kinase	SP1	specificity protein 1
rt-PA	recombinant tissue plasminogen activator	SPECT	single photon emission computed tomography
RT-PCR	reverse transcription polymerase chain reaction	SPG-II	spastic paraplegia type II
RyR	ryanodine receptor	SR-A	scavenger receptor type A
sALS	sporadic amyotrophic lateral sclerosis	SRBCs	sheep red blood cells
SAP	synapse-associated protein		

SREBP	sterol regulatory element binding protein	TOR1	target of rapamycin 1
SRF	serum-response factor	TRAF	TNF-receptor mediated factor
SSRI	selective serotonin reuptake inhibitors	TRAIL	TNF-related apoptosis inducing ligand (TNFSF10)
STAT	signal transducers and activators of transcription	TRANCE	TNF-related activation-induced cytokine (TNFSF11)
STP	short-term potentiation	TRANCER	TRANCE receptor (TNFRSF11A)
SV5	simian virus 5	TRE	tax responsive element
SVZ	subventricular zone	Treg	T regulatory cells
SWAP	short wavelength automated perimetry	Trk	receptor tyrosine kinase
T	tesla	TRP	transient receptor potential
TBE	tick-borne encephalitis virus	TSA	tissue-specific antigen
TBP	TATA-binding protein	Tyk2	protein tyrosine kinase 2
TCA	tricarboxylic acid	UACA	uveal autoantigen with coiled domains and ankyrin repeats
TCR	T-cell receptor	UMN	upper motor neuron
TCV	T cell vaccination	V1	primary visual cortex
TDO	tryptophan 2,3-dioxygenase	VAMP	vesicle-associated membrane protein
TE	echo time	VCAM	vascular cell adhesion molecule
TEC	thymic epithelial cell	VEGF	vascular endothelial growth factor
Teff	T effector cells	VEP	visual evoked potential
TF	transcription factor	VIP	vasoactive intestinal peptide
TG	trigeminal ganglia	VMAT-2	vesicular monoamine transporter-2 (solute carrier family 18; SLC18A2)
TGF	transforming growth factor	VZV	varicella-zoster virus
Th1	T helper type 1 cell	WKAH	Wistar-King-Aptekman-Hokudai
Th2	T helper type 2 cell	WNV	West Nile virus
TIA	transient ischemic attack	X-ALD	X-adrenoleukodystrophy
TIR	Toll/IL-1 receptor	XIAP	X-linked inhibitor of apoptosis protein
TJ	tight junction	ZO-1	zonula occludens-1 (TJP1)
TLR	toll-like receptor		
TMEV	Theiler's mouse encephalomyelitis virus		
TMT	trimethyltin		
TN	terminal nuclei		
TNF	tumor necrosis factor		
TNFR	tumor-necrosis factor receptor		

References

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