

Index

A

- Acquired demyelinating diseases. *See also specific diseases*
acute disseminated encephalomyelitis (ADEM), 600
central nervous system (CNS), 597–617
inflammatory, 598–600, 604–612, 615–617
mechanisms of myelin injury, 604–612
multiple sclerosis (MS), 598–599
myelin oligodendrocyte glycoprotein antibody disease (MOGAD), 599–600
neuromyelitis optica spectrum disorder (NMOSD), 599
noninflammatory, 600–604
osmotic myelinolysis, 603
overview, 598–604
progressive multifocal leukoencephalopathy (PML), 603–604
therapeutic strategies, 615–617
vitamin B12 deficiency, 600–603
- Acute disseminated encephalomyelitis (ADEM), 600
- Acute inflammatory demyelinating polyneuropathy (AIDP), 671–672
- Adaptive immunity, 605–607
- Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia, 645
- Adult polyglucosan body disease (APBD), 641
- Aging
in *C. elegans*, 17
and OPCs, 202–203
peripheral nerve changes with, 351–352
- Aicardi–Goutieres syndrome (AGS), 644–645
- Alexander disease, 184, 644
- ALS. *See* Amyotrophic lateral sclerosis
- Alzheimer’s Disease (AD)
Aqp4 mislocalization, 512
blood–brain barrier in, 433–434
cell–cell cross talk, 580–581
cerebral blood flow, 583
glial heterogeneity, 574–576
glial phagocytosis, lipid metabolism, and endolysosomal pathways, 576–581
glia–synapse phagocytosis, 578–579
microglial dysfunction, 369–370
neuronal excitability, 585–586
role of glia, 578
synapse elimination, 118–119
vascular pathologies as risk factors, 515
- Amyloidosis, 511–512, 515–516, 578–579
- Amyotrophic lateral sclerosis (ALS)
diseased astrocytes, 185–186
glial heterogeneity, 576
neuronal excitability, 586
perisynaptic Schwann cells as clinical target, 329–331
Antisense oligonucleotides, 647
- APBD (adult polyglucosan body disease), 641
- Aqp4 (aquaporin-4), 182, 426, 428, 433, 435, 509, 511–513, 516–517, 599–600
- Arachidonic acid–mediated neurovascular coupling, 140–142
- Astrocyte–astrocyte networks, and calcium signaling, 133
- Astrocyte heterogeneity
cell-extrinsic (neuronal) patterning of, 99–100
cell-intrinsic (developmental) patterning of, 99
functional, 96–97
introduction, 89–90
molecular, 94–96
morphological, 93–94
regional gene expression, 94–96
specification of, 97–100
technologies for discovering, 90–93
transgenic tools to manipulate subpopulations, 93
- Astrocyte reactivity
cancer, 183
context-specific regulation of, 180–181
definition, 174–175
discriminating astrocyte disease, 176
disease-associated gene mutations, 184–186
functions and effects of, 181
inflammation, 182–183
introduction, 173–174
nonproliferative and proliferative, 176–177
peripheral infection, 183–184
transcriptional and proteomic profiling, 177–180
triggers of, 175–176
- Astrocytes
blood–brain barrier, 417–418, 425–429
brain metabolism, 157–165
calcium signaling, 41–44, 125–134
cerebral blood flow regulation, 137–150
Drosophila, 27–28, 30–39, 41–46, 64–65
functional heterogeneity, 89–100
glioma-associated, 567–568
glutamate homeostasis, 585–586
glymphatic system, 511–513
heterogeneity of, 175–176
as interface cells, 157–159
as metabolic sensors, 164
molecular polymorphisms, 186
morphology, 157–159
in multiple sclerosis, 608–609, 610–611
neural circuitry, roles in, 81–82
phagocytosis in *Drosophila*, 38–39

Index

- Astrocytes (*Continued*)
 reactive, 173–187
 satellite glia similarities, 454
 synapse formation, maturation, and elimination, regulation of, 107–119
 zebrafish, 80–82
- Astrocytopathies, 644–645
- Autism spectrum disorders, blood–brain barrier dysregulation in, 436–437
- Autoimmune demyelination, 547–548
- Axons
 ensheathing glial response to injury in *Drosophila*, 39–40
 myelination (*see* Myelination)
 oligodendroglial support of function and integrity, 249–252
 outgrowth, role of microglia in, 394–395
 plasticity, OPC role in, 200
 protection by remyelination, 527
 regeneration (*see* Nerve regeneration)
 repairing demyelination in zebrafish, 76
 Schwann cell development, regulation of, 265–266
 Schwann cell regulation of survival, diameter, and transport, 273–274
- B**
- BAMs (border-associated macrophages), 368, 384, 386
- Barriers
 in *Drosophila*, 56–62
 functional, 56–62
 glial–ECM interactions, 60–62
- Basement membrane, of blood–brain barrier, 418–419
- BC (boundary cap) cells, 496–503
- Behavior
 and *Caenorhabditis elegans* glia, 15–17
 and *Drosophila* glia, 41–45
 governed by brain metabolism, 164–165
 microglial regulation, 401–402
- Blood–brain barrier (BBB)
 astrocyte, 417–418, 425–429
 basement membrane, 418–419
 brain metabolism, 159
 cells, 414–419
Drosophila, 55–56, 59
 dysfunction in central nervous system disorders, 430–438
 endothelial cells, 414–416
 features and molecules of the, 419–424
 immune cells, 418
 leukocyte adhesion molecules (LAMs), 423
 mural cells, 416–417
 overview, 413–414
 regulation of formation and homeostasis, 424–430
 tight junctions, 419–421, 435
 transcytosis, 422–423, 436
 transporters, 421–422, 436
- Blood–brain barrier regulation
 by astrocytes, 425–429
 barrier properties during angiogenesis, 424–425
 convergence of signaling events at the blood–brain barrier, 429–430
 by pericytes, 425
 traumatic brain injury, 434
- Blood–nerve barrier (BNB), 28, 274, 346, 498, 660
- Blood oxygenation level dependent (BOLD) effect, 140
- Border-associated macrophages (BAMs), 368, 384, 386
- Boundary cap (BC) cells, 496–503
- Brain clearance. *See* Waste clearance in the brain
- Brain colonization, by microglia in zebrafish, 77–78
- Brain metabolism
 anatomy, 159–160
 astrocytes, roles of, 157–165
 behavior governed by, 164–165
 building blocks, supply of, 162–163
 compartmentalization and energy reservoirs, 161
 dependent on neuronal activity, 161–162
 waste recycling, 163–164
- Bystander neurons, 65–66
- C**
- CADASIL (cerebral arteriopathy, autosomal-dominant, with subcortical infarcts and leukoencephalopathy), 646
- CADM3 mutations, 666
- Caenorhabditis elegans* glia
 animal behavior, functions in, 15–17
 axon guidance and brain assembly, 15
 cell polarity, 8
 cell size control, 8
 cell types, 2–5
 dendrite outgrowth, 14
 epithelial cells, glial functions of, 18–19
 further studies, 19
 general properties, 2–6
 heterogeneity, 5
 immunity, 17
 introduction, 1–2
 locomotion and salt resistance, 17
 longevity, 17–18
 membrane subdomains, 5–6
 morphogenesis, 8–13
 neurite specification, 14
 neurodegeneration, roles in, 13–14
 as neuronal progenitors, 13
 neuron morphology control, 14–15
 neuron-receptive ending (NRE) shape, 14
 ray sensilla morphogenesis, 15
 remodeling in dauers, 11, 13
 repetitive behavior, 17
 as sensory cells, 15–16
 sensory-neuron activity, regulation of, 16
 sexual dimorphism, 5
 shape maintenance, glial–epithelial interactions with, 9, 11
 sleep regulation, 16–17
 specification, 6–8
 stress and aging, roles in, 17

- synapse formation and maintenance, 15
 - synaptic activity, regulation of, 16–17
 - vertebrate glia, similarities to, 6
 - Calcium signaling
 - in *Drosophila*, 41–44, 65
 - enteric glia, 481–482
 - pathways in neurovascular coupling (NVC), 139–142
 - perisynaptic Schwann cell response to, 322–327
 - in satellite glia, 465–466
 - Calcium signaling, astrocyte
 - activation and silencing, 127–128
 - analyzing, 128
 - astrocyte–astrocyte networks, 133
 - consequences, 128–131
 - imaging, 126–127, 129, 132
 - overview, 125–126
 - relation to broader areas of biology, 131–133
 - speculation on, 131–133
 - CAMs. *See* Cell-adhesion molecules
 - Canavan disease, 643
 - Cancer
 - glial malignancies, 561–568
 - innervation, role of, 352
 - reactive astrocytes and, 183
 - Capillaries, classes of, 413–414
 - Cathepsin A, 647
 - CBF. *See* Cerebral blood flow
 - Cell-adhesion molecules (CAMs)
 - astrocytic, 114–115
 - nodes of Ranvier and, 296–298, 300–303
 - Central nervous system (CNS)
 - acquired demyelinating diseases of, 597–617
 - development and plasticity, role of microglia in, 383–402
 - disorders, astrocyte roles in, 173–187
 - glial regulation of energy supply, 581–584
 - microglia as integrative hubs of, 363–376
 - remyelination, 523–549
 - spatial patterning, 387–394
 - synaptic wiring, 394–400
 - Cerebral arteriopathy, autosomal-dominant, with
 - subcortical infarcts and leukoencephalopathy (CADASIL), 646
 - Cerebral blood flow (CBF)
 - astrocyte regulation, 137–150
 - bidirectional control of vessel diameter, 144–145
 - Ca²⁺ signaling, 137, 139–142, 144–147, 149–150
 - function hyperemia, 138–140
 - glial regulation of, 581–582
 - in neurodegenerative disease, 582–583
 - neurovascular coupling, 140–142
 - overview, 137–138
 - vascular cell involvement in flow, 514–515
 - Cerebrospinal fluid (CSF)
 - components of flow in brain, 511
 - drainage by meningeal lymphatics, 510, 516
 - glymphatic flow, 508–517
 - macrophage surveillance, 515–516
 - neuron, involvement in flow, 513–514
 - production, 507–508
 - Cerebrotendinous xanthomatosis (CTX), 642–643
 - Charcot–Marie–Tooth disease (CMT), 659–660, 663–671
 - Cholesterol, astrocyte-secreted, 112
 - Chromatin-remodeling complexes, 221
 - Chronic inflammatory demyelinating polyneuropathy (CIDP), 671
 - Chronic nerve injury, 350
 - Circadian rhythm regulation in *Drosophila*, 44
 - Claudins, 419–420
 - CMT (Charcot–Marie–Tooth) disease, 659–660, 663–671
 - CNS. *See* Central nervous system
 - Collagen chains, pathogenic variants in, 646–647
 - Congenital hypomyelinating neuropathy (CHN), 660
 - Contact-mediated mechanisms of astrocyte–synapse regulation, 113–115
 - Cortex glia, in *Drosophila*, 27–28, 30, 32–34, 40–41, 44–45
 - Cre/lox, to manipulate microglia function, 386–387
 - CSE. *See* Cerebrospinal fluid
 - CTCI* gene, 647
 - CTX (cerebrotendinous xanthomatosis), 642–643
 - Cytoskeletal barrier, 301–302
- D**
- Degeneration. *See also* Neurodegeneration
 - of nerve terminals, 319
 - Wallerian, 40, 250, 342, 350, 523
 - Déjérine–Sottas syndrome, 660
 - Demyelinating neuropathies
 - immune-mediated, 671
 - inherited, 659–671
 - as Schwann cell–autonomous, 660
 - Demyelination
 - acquired diseases, 597–617
 - consequences of chronic, 611–612
 - disorders of, 641–644
 - OPC response to injury, 202
 - remyelination as normal response to, 526–527
 - repairing axon in zebrafish, 76
 - transition zone, 501
 - Dendrites, astrocyte regulation of, 35–36
 - Depression, 585
 - Designer receptors exclusively activated by designer drugs (DREADDs), 127
 - Development
 - astrocyte–neuron contact during, 113–114
 - transition zone glia, 494–498
 - Diabetes, and blood flow dysregulation, 148–149
 - Disease. *See also specific diseases*
 - demyelinating diseases (*see* Acquired demyelinating diseases)
 - microglia and neuropsychiatric, 401–402
 - microglial dysfunction associated, 368–370
 - neurodegenerative (*see* Neurodegenerative diseases)
 - Dorsal entry zone (DREZ), 494–500, 502
 - Draper, 37–41, 46, 66, 116–117, 389
 - DREADDs (designer receptors exclusively activated by designer drugs), 127

Index

Drosophila glia

- astrocytes, 27–28, 30–39, 41–46
- Ca²⁺ signaling, 41–44
- cortex glia, 27–28, 30, 32–34, 40–41, 44–45
- ensheathing glia, 27–28, 30, 32–34, 38–40, 45–46
- as functional barriers, 56–62
- introduction, 27–28
- memory, regulation of, 44–45
- nervous system histology, 28–33
- neural circuit function and behavior, 41–45
- neuronal circuit remodeling and phagocytosis, 36–41
- regulation of neuron and neural circuit structure, 33–36
- as signaling intermediates, 62–66
- sleep and circadian behavior, 43–44

D-serine, 142

E

EETs (epoxyeicosatrienoic acids), 137, 139, 144, 149–150

Embryonic development, and astrocyte heterogeneity, 97–100

Endolysosomal pathways, 576–577

Endothelial cells, of blood–brain barrier, 414–416

Ensheathing glia, in *Drosophila*, 27–28, 30, 32–34, 38–40, 45–46, 55, 61

Enteric glia

- development and diversification, 476–479
- epithelial barrier and stem cell regulation, 483–484
- glia-to-neuron communication, 482
- gut microbes, interaction with, 483
- in gut pathophysiology, 484–486
- interactions with neurons, 479–482
- neuron-to-glia communication, 481–482

Enteric nervous system (ENS). *See also* Enteric glia

- glial differentiation and cell fate specification in, 477
- glial heterogeneity in, 477–479
- interactions between enteric glia and neurons, 479–482
- neurogenesis, 479
- overview, 475–476

Epilepsy

- blood flow dysregulation, 149
- neuronal excitability, 584–585, 587

Epithelial barrier, and enteric glia, 483–484

Epithelial cells, glial functions of *C. elegans*, 18–19

Epoxyeicosatrienoic acids (EETs), 137, 139, 144, 149–150

Extracellular vesicles, astrocyte, 111

F

Functional barriers, glia as, 56–62

Functional hyperemia, 138–140, 148–149

G

Gap junctions

- in *C. elegans*, 2, 14
- in *Drosophila*, 43, 58, 62
- in satellite glia, 453–454, 465–467

Gas exchange in *Drosophila*, 64–65

GBS (Guillain–Barré syndrome), 671–672

Gene therapy, for inherited white matter disorders, 647–648

Genetically encoded Ca²⁺ indicators (GEICs), 126, 128

Genetic leukoencephalopathies (gLEs). *See* Inherited white matter disorders (IWMDs)

GJB1 mutations, 666–667

Glia

- glial–ECM interactions, 60–62
- heterogeneity, 574–576
- migration, 60–62
- regulation of neuronal excitability, 584–587

Glial-lymphatic (glymphatic) system. *See* Glymphatic system

Glial sheath, formation in *Drosophila*, 56–62

Glioma

- architecture and physiology, 563–564
- astrocytes associated with, 567–568
- cellular subpopulations mimicking glia, 563
- classification, 561–562
- interactions with the brain microenvironment, 564–568
- neural stem cells, interaction with, 567
- neuron interactions, 564–566
- oligodendroglial lineage cells, 566–567
- overview, 561–563

Glutamate homeostasis, and astrocytes, 585–586

Glymphatic system

- astrocytes, 511–513
- phases of CSF flow, 508–509
- physiological processes driving fluid flow in, 513
- waste clearance in the brain, 507–517

Glypicans (GPCs), 110–111

Guillain–Barré syndrome (GBS), 671–672

Gut microbes, enteric glia interaction with, 483

H

Hereditary neuropathy with liability to pressure palsies (HNPP), 664–665

Heterogeneity, glia, 574

Histone acetyltransferases (HATs), 220

Histone deacetylases (HDACs), 220–221, 278–279

Histone methylation, 221

Huntington's disease

- blood–brain barrier dysregulation in, 437–438
- diseased astrocytes, 185
- neuronal excitability, 585–586

20-Hydroxyeicosatetraenoic acid (20-HETE), 137, 140, 144, 146, 149–150

Hyperemia, functional, 138–140, 148–149

Hypoglycemia, and blood flow dysregulation, 148–149

Hypomyelination, 639–641

Hypoxia, modulation of blood–brain barrier following, 434–435

I

IBD (inflammatory bowel disease), 484–486

IBS (irritable bowel syndrome), 484, 486

Imaging, of astrocyte calcium signals, 126–127, 129, 132

- Immune cells of blood–brain barrier, 418
 - Immune signaling, and oligodendrocyte precursor cells (OPCs), 201–202
 - Immune system
 - cross talk with microglia, 580–581
 - demyelinating neuropathies, 671
 - glioma interaction, 567
 - Infection, reactive astrocytes and peripheral, 183–184
 - Inflammation
 - demyelinating neuropathies, 671
 - enteric glia response to acute, 484–485
 - leptomeningeal, 611
 - reactive astrocytes and, 182
 - and remyelination, 530–531
 - satellite glia response, 467–468
 - Inflammatory bowel disease (IBD), 484–486
 - Inflammatory demyelinating diseases
 - mechanisms of myelin injury, 604–612
 - overview, 598–600
 - Inherited neuropathies
 - metabolic, 670
 - mutations involved, 660–671
 - myelin sheath disruption, 660–667
 - nodal region disruption, 667–668
 - nomenclature, 659–660
 - receptors, signaling, and endosomal trafficking associated, 668–670
 - table of, 661–662
 - transcription factor and promoter associated, 670–671
 - Inherited white matter disorders (IWMDs)
 - classification by cellular pathology, 639–647
 - clinical manifestations, 633–635
 - diagnosis, 638–639
 - overview, 631–632
 - therapies, 636–637, 647–648
 - types, 632, 638
 - Injury
 - chronic nerve, 350
 - glia as signaling intermediates, 65–66
 - mechanisms of myelin injury, 604–612
 - OPC response, 200
 - reactive astrocytes, 181–182
 - response of zebrafish glia, 82
 - satellite glia response, 467–468
 - Schwann cells in nerve repair, 341–353
 - synapse elimination, 118–119
 - synaptic repair, 319–322
 - transition zone glia response, 500
 - traumatic brain, 434
 - Innervation
 - cancer, role in, 352
 - tissue homeostasis and regeneration, role in, 348–349
 - Internodes, 294, 296–297
 - Ion channels
 - blood–brain barrier, 436
 - nodes of Ranvier, 273, 293–294, 296–304
 - IPSC-derived approaches to study microglia, 372
 - Irritable bowel syndrome (IBS), 484, 486
 - Ischemia, modulation of blood–brain barrier following, 434–435
 - IWMDs. *See* Inherited white matter disorders
- ## J
- Junctional adhesion molecules (JAMs), 419–421
 - Juxtaparanodes (JXPs), 294, 296–298, 301–302
- ## K
- Krabbe disease, 645–646
- ## L
- Leptomeningeal inflammation, 611
 - Leptomeningeal stroma, 516–517
 - Leukoaxonopathies, 640–641
 - Leukocyte adhesion molecules (LAMs), 423
 - Leukodystrophies (LDs). *See* Inherited white matter disorders (IWMDs)
 - Leukoencephalopathy with calcifications and cysts (LCC), 647
 - Leukovascularopathies, 646–647
 - Limb regeneration, 348
 - Lipids
 - astrocyte-derived, 112
 - glial metabolism, 576–577
 - Lymphatics, meningeal, 510–511, 516
- ## M
- Macrophages
 - CSF flow, role in, 515–516
 - in multiple sclerosis, 610–611
 - MAG mutations, 665–666
 - Magnetic resonance imaging, 525
 - Malignancies, glial, 561–568
 - MAPK signaling, and oligodendrocyte differentiation, 225–226
 - Maternal immune activation (MIA), 394, 402
 - Matrix metalloproteases (MMPs), 432–438
 - Memory, regulation of *Drosophila*, 44–45
 - Meningeal lymphatics, 510–511, 516
 - MEP (motor exit point), 494–500
 - Metabolism
 - brain (*see* Brain metabolism)
 - lipid, 576–577
 - mutations and demyelinating neuropathy, 670
 - Metabolite transport, 159–160
 - Metachromatic leukodystrophy, 642
 - Methylation, histone, 221
 - MIA (maternal immune activation), 394, 402
 - Microglia
 - across the life span, 363–364
 - axon outgrowth and synaptogenesis, 394–395
 - behavior regulation, 401–402
 - brain colonization, 77–78

Index

- Microglia (*Continued*)
- cre/lox technology to manipulate microglia function, 386–387
 - engulfment mechanisms, 387–391
 - functional states, 385
 - functions needed for healthy brain function, 368–370
 - glia-synapse phagocytosis in neurodegeneration, 578–580
 - glioma-associated, 567
 - how to study human, 370–376
 - hubs for external and local signals, 365–368
 - immune cell cross talk, 580–581
 - as integrative hubs of the CNS, 363–376
 - interaction with other glia, 78
 - modulation of synaptic function, 400
 - in multiple sclerosis, 607–608, 610–611
 - and neuroinflammation, 580
 - neuron removal, 79–80
 - ontogeny, 384
 - regulation of cell survival, proliferation, and differentiation, 391–392
 - specific markers, 386
 - synaptic pruning, 395–400
 - synaptic remodeling, 395–400
 - synaptic wiring in CNS, 394–400
 - tools for studying, 384–387
 - transcriptional and functional heterogeneity, 78–79
 - vasculature regulation, 393–394
 - white matter, role in, 392–393
 - zebrafish, 77–80
- Microglia depletion, 387
- Microgliopathies, 645–646
- MMPs (matrix metalloproteinases), 432–438
- MOGAD (myelin oligodendrocyte glycoprotein antibody disease), 599–600
- Monocarboxylate transporter 8 (MCT8) deficiency syndrome, 640
- Motor exit point (MEP), 494–500
- MPZ mutations, 665
- Multiple sclerosis (MS)
- blood–brain barrier in, 430–433
 - cell-based remyelination, 547–548
 - glial heterogeneity, 576
 - myelin injury in progressive forms, 609–612
 - myelin injury in relapsing, 605–609
 - neuronal excitability, 587
 - overview, 598–599
 - remyelination in, 612–615
 - therapeutic strategies, 615–617
- Mural cells, of blood–brain barrier, 416–417
- Myelin
- formation, 246–249
 - gene expression, 214
 - injury in multiple sclerosis, 605–612
 - peripheral nervous system (PNS) diseases, 659–672
 - structure, 244–246
 - vacuolation, 643–644
- Myelinated axons
- maintaining excitable domains in, 302–304
 - organization of, 293–298
- Myelination. *See also* Remyelination
- adaptive, 74
 - epigenetic control, 220–222
 - ligand-receptors inhibiting, 223–224
 - ligand-receptors promoting, 224–225
 - markers of myelinating oligodendrocytes, 217
 - Schwann cell (*see* Schwann cell myelination)
 - transcription factors promoting differentiation, 219–220
 - zebrafish, 74–76
- Myelinogenesis
- cell-based therapies for, 543–548
 - normal, 612
- Myelin oligodendrocyte glycoprotein antibody disease (MOGAD), 599–600
- Myelin plasticity
- experience-dependent, 253–254
 - neural activity-dependent, 254–255
 - overview, 252–253
- Myelin sheath
- genetic disruptions of, 660–667
 - morphogenesis, 268
 - organization of the myelinating Schwann cell, 269–273
 - regulation thickness and internode length, 268–269
- N**
- NCCs. *See* Neural crest cells
- Nerve barrier, in *Drosophila*, 28, 55–56, 59
- Nerve injury
- chronic, 350
 - perisynaptic Schwann cells, 317, 319–322, 332, 346
 - satellite glia response, 342, 467–468
 - Schwann cells, 350–351, 353
- Nerve regeneration
- bridge/wounds site, 345
 - distal nerve stump, 345–346
 - pathologies from aberrant repair, 349–353
 - restoration of nerve function, 347–348
 - satellite glial cells, 342
 - Schwann cells, 343–348
 - terminal glia, 346–347
 - transition zone glia, 500
- Neural circuit structure, in *Drosophila*, 33–36
- Neural crest cells (NCCs)
- enteric glia, 476–477, 479
 - glia at transition zone, 494–497
 - Purkinje cells, 417
 - satellite glia development, 342, 462–463
 - Schwann cells, 263–264, 275–277
 - transition zone, 494–497
- Neural progenitor cells (NPCs), 390–391
- Neural stem cells (NSCs)
- glioma interaction, 567
 - regional heterogeneity, 97–98
 - temporal heterogeneity, 98–99
- Neuregulin 1 (NRG1), 316–317, 321, 347, 462
- Neurodegeneration

- Caenorhabditis elegans*, 13–14
 - cell–cell cross talk, 580–581
 - energy supply, defects in, 581–584
 - glial phagocytosis in *Drosophila*, 37
 - glia–synapse phagocytosis in, 578–580
 - Neurodegenerative diseases
 - blood–brain barrier modulation in, 430–434
 - glial heterogeneity, 574–576
 - glial phagocytosis, lipid metabolism, and endolysosomal pathways, 576–581
 - neuronal excitability, 584–587
 - overview, 573
 - Neurodevelopmental disorders
 - astrocyte-secreted factors and, 112–113
 - modulation of the blood–brain barrier in, 436–438
 - Neurofibromatosis type 1 (NF1), 349, 353, 501–502, 567
 - Neurogenesis, and enteric nervous system, 479
 - Neuro–glia–vascular unit, 157
 - Neuroinflammation, 580
 - Neuromuscular junction (NMJ)
 - perisynaptic Schwann cells, role of, 311–333
 - repair and remodeling, 319–322
 - synaptogenesis, 316–318
 - tripartite organization of vertebrate, 312–316
 - Neuromyelitis optica (NMO), 430–433
 - Neuromyelitis optica spectrum disorder (NMSOD), 599
 - Neuronal circuits
 - astrocytes role in, 107–119
 - remodeling in *Drosophila*, 36–41
 - Neuronal corpses, detection by cortex glia in *Drosophila*, 40–41
 - Neuronal excitability, glial regulation of, 584–587
 - Neuronal remodeling, in *Drosophila*, 36–41
 - Neurons
 - CSF flow, involvement in, 513–514
 - disorders caused by a decrease in glial energetic support, 583–584
 - enteric glia interactions with, 479–482
 - glioma interactions, 564–566
 - removal by microglia in zebrafish, 79–80
 - survival and maturation, role of enteric glia in, 481
 - transition zone glia role in development and organization, 500
 - Neuropathology, OPCs in, 202
 - Neuropathy, peripheral, 350–351
 - Neuropsychiatric symptoms and disorders, microglial contributions to, 401–402
 - Neurotransmitter degradation, 480–481
 - Neurotransmitter synthesis, 480
 - Neurovascular coupling (NVC)
 - arachidonic acid–mediated, 140–142
 - Ca²⁺-dependent signaling pathways, 139–142
 - cerebrospinal fluid flow, 514
 - overview, 137, 140
 - NF1 (neurofibromatosis type 1), 349, 353, 501–502, 567
 - Nitric oxide (NO)
 - enteric glia, 480
 - vascular tone, effect on, 144, 146, 149
 - NMJ. *See* Neuromuscular junction
 - NMO (neuromyelitis optica), 430–433
 - NMSOD (neuromyelitis optica spectrum disorder), 599
 - Nodes of Ranvier
 - assembly, 298–302
 - CAM-mediated formation of cytoskeletal barrier at the paranodal junction, 301–302
 - composition, 296–298
 - disruption of nodal components, 667–668
 - extrinsic regulators of node formation, 299
 - intrinsic regulators of node formation, 298–299
 - molecular organization of the nodal region, 666–667
 - morphology, 293–296
 - nodal axoglial interactions, 299–301
 - NPCs (neural progenitor cells), 390–391
 - NRG1 (neuregulin 1), 316–317, 321
 - NSCs. *See* Neural stem cells
 - NVC. *See* Neurovascular coupling
- O**
- Occludin, 420
 - Oligodendrocyte differentiation
 - epigenetic control, 220–222
 - intracellular signaling pathways, 225–230
 - ligand–receptors inhibiting, 223–224
 - ligand–receptors promoting, 224–225
 - markers, 216–217
 - membrane expansion, 215–216
 - morphological, 214
 - myelin gene expression, 214
 - regulators of, 211–230
 - single-cell approaches to study, 217
 - transcriptional control of oligodendrocyte development and myelination, 218–222
 - Oligodendrocyte precursor cells (OPCs)
 - in axon plasticity, phagocytosis, and immune signaling, 200–202
 - cell cycle exit, 213–214, 216–217
 - development and fate, 194–195
 - differentiation of, 211–230
 - discovery of, 193–194
 - generation of oligodendrocytes, 197–198
 - glioma interactions, 562–563, 566–567
 - markers, 216
 - in multiple sclerosis, 609
 - in neuropathology and aging, 202–203
 - phagocytosis, 200–201
 - pluripotent stem cell–derived hOPCs, 539–543
 - remyelination, roles in, 527–535, 537, 539–541, 543–545, 548
 - remyelination failure in multiple sclerosis, 615
 - residency and morphology, 195–197
 - specification and proliferation of, 212–213
 - synapse elimination by, 117–118
 - synaptic input to, 198–200
 - transcription factors maintaining OPCs in the precursor state, 218–219
 - zebrafish, 72–77

Index

- Oligodendrocytes
 - intrinsic and adaptive generation, 197–198
 - in multiple sclerosis, 609
 - myelination, 243–256
 - support of axon function and integrity, 249–252
 - zebrafish, 72–77
- Oligodendrocytopathies, 639–644
- OPCs. *See* Oligodendrocyte precursor cells
- Osmotic myelinolysis, 603

- P**
- Pain, in failed nerve repair, 351
- Paranodal axoglial junctions (PNJs), 293–294, 296–297, 299–302
- Parkinson's disease
 - blood–brain barrier in, 434
 - cerebral blood flow, 583
 - synapse elimination, 118–119
- Pelizaeus–Merzbacher disease (PMD), 639
- Pericytes (PCs)
 - blood–brain barrier, 416–417, 425
 - during stroke, 582–583
- Perineurial glia, 43, 56–62, 497–498, 500–501
- Peripheral myelin protein 22 kDa (PMP22), 660, 663–665
- Peripheral nerves
 - aging, 351–352
 - architecture, Schwann cell regulation of, 274–275
 - nerve repair, 341–353
 - structure in homeostasis and following injury, 343
- Peripheral nervous system
 - architecture of the myelinated axon in the, 664
 - myelin diseases, 659–672
- Peripheral neuropathies, 350–351
- Perisynaptic Schwann cells (PSCs)
 - decoding of synaptic properties and activity, 324–327
 - maladapted properties in diseases, 327–331
 - overview, 311–312
 - plasticity of PSC properties, 327
 - synaptic maintenance, 318
 - synaptic remodeling, 318–319
 - synaptic repair, 319–322
 - synaptic transmission, detection of, 322–324
 - synaptogenesis, role in, 316–318
 - tripartite organization of neuromuscular junction, 312–316
- PGE₂ (prostaglandin E₂), 137, 144, 149–150
- Phagocytosis
 - in *Drosophila*, 37–41
 - glial and Alzheimer's disease, 576–579
 - glia-synapse phagocytosis in neurodegeneration, 578–580
 - by microglia, 368, 389–390, 392, 399, 401
 - by perisynaptic Schwann cells, 319
 - synapse elimination, 116–119
- Phagocytosis in *Drosophila*
 - by astrocytes, 38–39
 - by cortex glia, 40–41
 - by ensheathing glia, 39–40
 - overview, 37
- Phenylketonuria (PKU), 643–644
- PI3K/AKT/mTOR signaling, in oligodendrocyte differentiation, 229
- Plaque formation/clearance, role of glia in, 578
- Plasticity
 - glial regulation of neurite structure, 35–36
 - myelin, 252–255
- Pleated septate junctions, 59
- PMD (Pelizaeus–Merzbacher disease), 639
- PMP22 (peripheral myelin protein 22 kDa), 660, 663–665
- PNJs (paranodal axoglial junctions), 293–294, 296–297, 299–302
- POLR3-related disorder, 639–640
- Positron emission tomography, 526
- Potassium
 - cerebral blood flow, effect on, 139, 142
 - K⁺ and brain metabolism, 161–162
- Programmed cell death, microglial control of, 387–390
- Progressive multifocal leukoencephalopathy (PML), 603–604
- Prostaglandin E₂ (PGE₂), 137, 144, 149–150
- Pruning
 - by microglia, 395–400
 - microglia role in, 80
- PSCs. *See* Perisynaptic Schwann cells

- R**
- Radial glia
 - Caenorhabditis elegans* homology, 6, 13, 18
 - zebrafish, 81–82
- Reactive astrocytes, 173–187
 - astrocyte-mediated non-cell-autonomous dysfunction or degeneration, 186
 - in neurodegenerative diseases, 575–576
 - therapeutic targeting of, 186–187
 - transcriptional and proteomic profiling, 177–180
 - in traumatic injury and stroke, 181–182
- Remyelination
 - of central nervous system axons by Schwann cells, 531
 - disease-associated modulators, 613–615
 - enhancing endogenous, 534–537
 - failure, causes of, 531–534
 - function restored by, 527
 - by glial progenitor cell transplantation, 537–539
 - identifying in animal models, 523–525
 - identifying in humans, 525–526
 - and inflammation, 530–531
 - mechanisms of, 527–531
 - as normal response to demyelination, 526–527
 - oligodendrocyte precursor cells (OPCs), 527–535, 537, 538–541, 543–545, 548
 - pluripotent stem cells as a source of myelinogenic progenitors, 539–543
 - successful, 612–613
 - targets of therapies for, 543–548
 - therapeutic strategies, 615–617

Repetitive behavior, in *C. elegans*, 17
RNAs, noncoding, 221–222

S

Satellite glial cells (SGCs)

antibodies, 456–461
common functionalities, 464–466
development and plasticity, 462–464
mouse lines, 455
nerve regeneration, 342
nervous system function, effects on, 466–467
nervous system pathology, 467–468
overview, 453–462
pair response, 351
tissue-specific differences, 464–466

Schizophrenia, 402, 437

Schwann cell development

axonal signals, 265–266
basal lamina signals, 266–267
mechanisms of Schwann cell ensheathment and radial sorting, 267–268
stages of, 263–265
transcriptional and epigenetic regulation, 275–280

Schwann cell myelination

morphogenesis of myelin sheath, 268
organization of myelinating Schwann cell and myelin sheath, 269–273
regulation of myelin sheath thickness and internode length, 268–269

Schwann cell precursors (SCPs), in the enteric nervous system, 479

Schwann cells

endosomal signaling in, 669–670
extracellular matrix receptors of myelinating, 668–669
in nerve repair, 341–353
nociceptive, 351
pathologies from aberrant repair, 349–353
peripheral nerves architecture, regulation of, 274–275
perisynaptic, 311–333
regulation of axon survival, diameter, and transport, 273–274
remyelination of central nervous system axons, 531
terminal glia, 346–347
tissue homeostasis and regeneration, role in, 348–349
tumors, 349, 353

Seizures, and neuronal excitability, 584–585, 587

Sexual dimorphism, in *Caenorhabditis elegans* glia, 5

SGCs. *See* Satellite glial cells

Signaling intermediaries

in *Drosophila*, 62–66
during nervous system development, 62–64
during nervous system function and during injury, 64–66

Single-cell RNA sequencing (scRNA-seq)

astrocytes heterogeneity mapping, 90–91
blood–brain barrier gene expression studies, 423

enteric glia, 478

glial heterogeneity, 574
for microglial studies, 371, 384–386

Single-cell transcriptomics, 90–91

Single-nuclei RNA sequencing (snRNA-seq)

blood–brain barrier gene expression studies, 423
glial heterogeneity, 574, 576
for microglial studies, 371

Sleep

CSF flow, driver of, 513–514
regulation in *C. elegans*, 16–17
regulation in *Drosophila*, 43–44

SPARC, 111–112

Spatial patterning, in the developing and mature CNS, 387–394

Spatial transcriptomics, and astrocyte heterogeneity mapping, 91–93

Stem cells

myelogenic progenitors, 539–543
neural (*see* Neural stem cells)
therapies for multiple sclerosis, 617

Stress, in *C. elegans*, 17

Stroke

blood flow dysregulation, 149–150
endothelial transcytosis following, 436
modulation of blood–brain barrier following, 434–435
neuronal excitability, 586
reactive astrocytes, 181–182
spreading depression, 582–583

Synapse elimination

astrocyte control of, 115–119
in diseased/injured brains, 118–119
glia-synapse phagocytosis in neurodegeneration, 578–580
during the normal synapse remodeling, 117–118

Synapse formation

astrocyte-secreted factors, 108–113
contact-mediated mechanisms, 113–115
glypicans, 110–111
thrombospondins, 109–110

Synapse maturation

chordin-like 1 induction of, 112
SPARC, role of, 111–112

Synapse number

excitatory, 113–114
glial regulation in *Drosophila*, 34–35
inhibitory, 114–115, 400

Synaptic activity

decoding by perisynaptic Schwann cells, 324–327
modulation by perisynaptic Schwann cells, 325–326
perisynaptic Schwann cells integration of, 331–332

Synaptic function, microglial modulation of, 400

Synaptic maintenance, 318

Synaptic plasticity, 325–327

Synaptic pruning, by microglia, 395–400

Synaptic refinement, 395–400

Index

Synaptic remodeling, 117–118, 318–319, 395–400
Synaptic repair, 319–322
Synaptic transmission, PSC detection of, 322–324
Synaptic wiring in the CNS, 394
Synaptogenesis
 microglia, role of, 394–395
 role of perisynaptic Schwann cells in, 316–318

T

Terminal glia, 346–347
Therapeutics
 acquired demyelinating diseases, 615–617
 cell-based for myelinogenesis, 543–548
 inherited white matter disorders, 636–637, 647–648
 targeting reactive astrocytes, 186–187
Thrombospondins (TSPs), 109–110
Tight junctions (TJs), of blood–brain barrier,
 419–421, 435
Tissue regeneration, 348–349
Transcriptomic profiling of astrocytes, 94–95
Transcytosis, 422–423, 436
Transition zone glia
 CNS and pia matter–derived glia at the motor exit
 point, 497
 as CNS–PNS boundary, 499–500
 development and differentiation, 494–498
 functional importance of, 498–500
 in injury and disease, 500–502
 motor exit point (MEP), 494–500
 in neuronal development and organization, 500
 overview, 493–494
 perineurial glia, 497–498
 as progenitor cells, 498–499
Transition zones (TZs)
 boundary cap (BC) cells, 496–503
 comparison of vertebrate, 496, 498
 developmental origin and differentiation, 494–498
 overview, 493–494
Transporters, of blood–brain barrier, 421–422, 436
Traumatic brain injury, 434
Tripartite synapse, 159
TSPs (thrombospondins), 109–110
TUBB4A-related LD, 641

V

Vanishing white matter disease (VWMD), 644
Vascular cells, and CSF flow, 514–515
Vascular smooth muscle cells (VSMCs), 416, 418, 511, 515
Vasculature
 astrocyte regulation of tone, 146–147
 bidirectional control of vessel diameter, 144–145
 microglial role in regulating, 393–394
Vitamin B12 (cobalamin) deficiency, 600–603

W

Wallerian degeneration, 40, 250, 342, 350, 523
Waste clearance in the brain
 anatomy of, 507–511
 astrocytes, 511–513
 leptomeningeal stroma, 516–517
 macrophages, 515–516
 meningeal lymphatics, 510–511, 516
 neurons, 513–514
 vascular cells, 514–515
Waste recycling, and brain metabolism, 163–164
White matter
 IWMDs (*see* Inherited white matter disorders)
 role of microglia in, 392–393
 vanishing white matter disease (VWMD), 644
Wrapping glia, 28, 30, 55, 61–64

X

X-linked adrenoleukodystrophy (X-ALD), 641–642

Z

Zebrafish
 astrocytes, 80–82
 future research directions, 82–83
 introduction, 71–72
 microglia, 77–80
 oligodendrocytes, 72–77
 radial glia, 81–82
 transition zone studies, 494–500, 502–503