

## Index

- ADEM (acute disseminated encephalomyelitis), 118
- acute hemorrhagic leukoencephalitis, 119
- histological characteristics, 119
- relationship to infection, 118
- adhesion molecules
  - expression by oligodendrocytes, 129
  - F3, 129
  - ICAM-1, 129
  - integrins, 129
  - N-CAM, 129
  - PSA-NCAM, 129
  - VCAM-1, 129
- adrenoleukodystrophy, 116
- immunopathogenesis, 116
- adult stem cells
  - use in therapeutic myelin repair, 152
- aging
  - myelin and oligodendrocyte changes, 167
- Akt
  - regulation of myelin thickness, 99
- Alexander disease
  - inherited primary demyelinating disease, 138
- AMPA receptor
  - antagonists, 192
  - expression by oligodendrocytes, 191, 192
- ankyrin<sub>G</sub>, 78
  - targeting of sodium channels, 78
- antigen-presenting cells (APCs)
  - oligodendrocytes as APCs, 131
- apoptosis
  - mitochondrial pathway, 174
  - molecular pathways, 174
  - morphology of cells, 174
  - in MS, 174
  - oligodendrocyte apoptosis in SCI, 159
  - TRAIL pathway, 174
- AQP4, *see* aquaporin-4
- aquaporin-4
  - autoimmune target in NMO, 119
  - expression in the CNS, 119
- astrocytes, 50
- autoantibodies, 121
  - augmentation of EAE, 134
  - in CSF and serum of MS patients, 178
  - induction of remyelination, 134
  - in MS, 178
  - in NMO, 119
  - remyelination, 144, 178
  - role in myelin breakdown, 178
- autocrine survival loop
  - survival of immature Schwann cells: BDNF, IGF-2, PDGF-B, NT-3, LIF, 27
- axo-glial junction, 80
  - contactin, Capsr, NF155, 80
  - NF155, 80
  - non-compact myelin, 5
  - paranode
    - juxtaparanode, 5
- axonal damage, 179
  - as a result of myelin loss, 150
  - consideration in stem cell therapy, 148
  - density in MS plaques, 117
  - during the course of autoimmune demyelination, 135
  - interaction between
    - oligodendrocytes and axons, 101
  - transection in MS, 116
- axonal degeneration, 97
  - PLP-null mice, 101
- axonal regeneration
  - anti-Nogo antibodies, 40
  - CNS vs PNS, 43

- effect of MAG, 41
- inhibitors, 39
- NgR1, 42
- Nogo, 39
- Nogo knockouts, 41
- Schwann cells, 44
- B cells, 134
  - depletion therapy for MS, 134
  - myelin reactive antibodies, 134
  - rituximab, 134
- BACE1
  - regulation of myelin thickness, 98
- Baló's concentric sclerosis, 16, 173
  - upregulation of ischemic preconditioning transcription factors, 180
- Bands of Büngner
  - formation after nerve injury, 44
- basic helix-loop-helix (bHLH)
  - transcription factors
    - Olig1, 103
    - Olig2, 103
- blood-brain barrier, 135
- bone marrow-derived stem cells
  - autologous transplantation, 147
- bone morphogenetic proteins
  - inhibition of OPC development, 53
- bone-marrow-derived stem cells
  - fusion with target cells, 153
  - immunosuppressive properties, 152
  - lesional targeting via circulation, 153
  - neuroprotective properties, 152
  - therapy in MS, 153
  - transdifferentiation into oligodendrocytes, 152
  - use in therapeutic myelin repair, 152
- boundary capping cells
  - progenitors of Schwann cells, 25
- Caspr
  - binding partner of NF155, 80
- CD3<sup>+</sup> T cells
  - NMO, 119
- CD4<sup>+</sup> T cells
  - activation by cytokines, 121
  - activation of macrophages, 132
  - direct effects on oligodendrocytes, 134
  - interaction with oligodendrocytes, 120
  - myelin reactive, 176
  - upregulation of CD56, 120
- CD8<sup>+</sup> T cells
  - activation by cytokines, 121
  - interaction with oligodendrocytes, 120
- lysis of oligodendrocytes, 134, 177
- myelin reactive, 176
- NMO, 119
- cell therapies. *see also* therapeutic myelin repair
- cerebral palsy, 187
- chemokine receptors
  - CCR3, 124
  - CCR5, 127
  - CXCR1,2,3,4, 127
  - expression by oligodendrocytes, 124,
- chemokines, 44, 46, 123
  - CXCL1, 123
  - CXCL12, 124
  - production in the CNS, 123
  - transcription after TLR activation, 125
  - upregulation by IFN- $\gamma$ , 124, 179
- claudin-11
  - paranodal loops, 79
  - tight junctions, 75
- cluster of differentiation
  - CD9, 126
  - CD13, 126
  - CD15, 126
  - CD38, 126
  - CD44, 126
  - CD45, 126
  - CD56, 126
  - CD59, 126
  - CD81, 127
  - CD88, 127
  - CD95, 127
  - CD100, 127
  - CD140, 127
  - CD156, 127
  - CD200, 127
  - CD antigens, 125
  - recognition by monoclonal antibodies, 125
- CNP, 79, 81
  - functions in non-compact myelin, 76
- CNS myelin
  - radial component, 19
- compact myelin, 4, 65
  - cholesterol, 69
  - DM20, 71
  - intraperiod lines, 70
  - major dense lines, 70
  - major proteins, 70
  - MBP, 72
  - MOBPs, 73
  - myelin-specific components, 33
  - P0, 34
  - PLP, 33
  - radial component, 74

- complement
  - C1q binding to MOG, 130
  - C1q-C9 immunoreactivities in MS lesions, 130
  - complement-activated oligodendrocytes in MS lesions, 130
  - glutamate sensitization of oligodendrocytes, 130
  - in MS, 178
  - oligodendrocyte interactions, 130
  - sublytic complement activation, 130
- conduction velocity
  - giant axons, 8
  - myelination, 8
- connexins
  - Cx32, Cx47, Cx29, 77
  - formation of gap junctions, 77
- contactin
  - binding partner of NF155, 80
- contusion injury
  - characteristics, 154
- corticosteroids
  - effects on oligodendrocytes, 128
  - interaction with NF- $\kappa$ B, 128
- Cx32
  - mutations, 77
  - paranodal loops, 79
  - peripheral neuropathy, 37
  - X-linked Charcot-Marie-Tooth, 77
- Cx47, 77
- CXCL1
  - enhancement of OPC proliferative response, 123
  - expression by astrocytes, 124
  - OPC recruitment, 124
- CXCL12
  - regulation of oligodendroglial proliferation, 124
- cytokine receptors
  - expression by oligodendrocytes, 121, 179
  - for interleukins and IFN- $\gamma$ , 179
- cytokines
  - cross-talk between CNS and immune system, 17
  - IFN- $\beta$ 
    - effects on oligodendrocytes, 122
    - use as MS therapy, 122
  - IFN- $\gamma$ , 122
    - role in MS and EAE, 179
  - IL-6
    - oligodendrocyte and neuron survival, 121
  - IL-17, 134
  - IL-18
    - expression by oligodendrocytes, 121
  - inhibition in MS treatments, 117
  - interleukin-1, 121
  - LIF, 123
  - role in myelin/oligodendrocyte injury, 121
  - role in oligodendrocyte injury, 179
  - secretion by glia, 121
  - TGF- $\beta$ , 122
  - Th1 pro-inflammatory, 134
  - Th17 pro-inflammatory, 134
  - TNF- $\alpha$ , 46, 122
  - upregulation in injured nerve
    - NGF, BDNF, GDNF, IGF, 46
- demyelination
  - active demyelination, 116, 173
  - ADEM, 119
  - differentiation of NG2<sup>+</sup> cells following, 14
  - effects of persistent demyelination, 139
  - functional consequences, 138
  - heterogeneous mechanisms, 174
  - neuromyelitis optica, 119
  - patterns in MS lesions, 116
  - primary, 138
  - proximity to areas of remyelination, 184
  - repair after damage, 139
  - as a result of oligodendrocyte damage, 138
  - role of MAC, 132, 178
  - role of pathogenic antibodies, 178
  - role of pathogenic autoantibodies, 132
    - after SCI, 162, 165
    - secondary, 138
    - secondary spinal cord injury, 158
  - development of oligodendrocytes
    - growth factors, 59
    - injury and implications in hypomyelination, 189
    - peak vulnerability to PVL, 189
    - pre-oligodendrocytes and immature oligodendrocytes, 189
  - Devic disease. *see* neuromyelitis optica
  - discovery of the oligodendrocyte, 2
    - Ramón y Cajal, 2
    - Rio del Horteiga, 2
    - W. Ford Robertson, 2
    - Wilder Penfield, 2
  - DM20, 71
    - functions, 71
  - domain specific targeting
    - TGN, 90

- EAE  
 depletion of NK cells, 177  
 immune response against MOG, 131  
 induction in TNF- $\alpha$  knockouts, 122  
 macrophage depletion, 132  
 as a model for ADEM, 119  
 as a model of autoimmunity, 133  
 in PLP/SOCS1 transgenics, 124  
 role of anti-myelin antibodies, 134, 178  
 role of CD8<sup>+</sup> cells, 134  
 role of CD200-CD200R, 127  
 role of cellular response, 175  
 role of complement, 130  
 role of glutamate excitotoxicity, 181  
 role of glutamate toxicity, 130  
 role of IFN- $\gamma$ , 179  
 role of MAC, 178  
 role of reactive oxygen species, 182  
 role of TNF- $\alpha$ , 122, 129  
 role of TRAIL system, 175  
 treatment with AMPA/kainate antagonists, 128
- electrical activity  
 affect on myelination, 29
- embryonic stem cells  
 ethical problems, 151  
 tumor formation after transplant, 147, 152  
 use in therapeutic myelin repair, 146, 151
- endogenous neural precursors  
 response in MS, 142
- eosinophils  
 NMO, 119
- evolution of myelin, 8, 64
- excitotoxicity  
 effect on oligodendrocytes processes, 194  
 glutamate, 186  
 implications in oligodendrocyte death, 186  
 role in periventricular leukomalacia (PVL), 186, 190  
 in SCI, 159
- experimental autoimmune encephalomyelitis. *see* EAE
- FGF2  
 mitogen for NG2<sup>+</sup> cells, 164
- fingolimod  
 multiple sclerosis  
 drug treatments, 117
- GalC  
 paranodal loop formation, 79
- genetic diseases  
 Canavan disease, 109  
 childhood ataxia with CNS hypomyelination (CACH), 109  
 Krabbe, 109  
 mutations in myelin genes, 106  
 mutations in non-myelin genes, 109  
 Pelizaeus-Merzbacher Disease, 78, 92, 108  
 spastic paraplegia type 2 (SPG2), 108  
 susceptibility to schizophrenia, 110  
 therapeutic intervention, 110  
 X-linked adrenoleukodystrophy (ALD), 109  
 X-linked Charcot-Marie-Tooth, 77
- genetic diseases affecting oligodendrocytes. *see* genetic diseases
- genome-wide association studies  
 discovery of genes linked to multiple sclerosis, 105
- genomic screening  
 identification of genes involved in disorders, 9
- genomics, 64  
 applications in oligodendrocyte biology, 104
- glatiramer acetate  
 multiple sclerosis  
 drug treatments, 117
- gliomedins  
 role in Na<sup>+</sup> channel clustering, 36
- glutamate  
 damage in MS, 180  
 extracellular sources, 196  
 metabolism, role in MS, 127  
 role in SCI, 159
- glutamate receptors, 180  
 AMPA/kainate-mediated excitotoxicity, 127  
 expression by oligodendrocytes, 180  
 ionotropic, 186  
 metabotropic, 186
- glutamate transporters, 196, 199  
 glial, 196  
 GLT1, 197  
 neuronal, 196  
 regulation of glutamate concentration, 186  
 role in production of extracellular glutamate, 196
- glutamatergic signaling  
 role in developing cerebral white matter, 198
- GOLLI  
 gene of the oligodendrocyte lineage, 72
- g-ratio, 96

- gray matter diseases
  - role of oligodendrocytes in, 9
- growth factors in OPC differentiation
  - IGF, thyroid hormone, 59
- HERV-W
  - role in MS, 134
- histotoxic hypoxia
  - pattern III MS lesion, 179
  - subset of MS lesions, 179
- hypoxia
  - in PVL, 189
- hypoxic-ischemia, 190
  - models in oligodendrocytes, 191
  - production of extracellular glutamate, 190
- IFN- $\beta$ 
  - effects on oligodendrocytes, 122
  - effects on remyelination, 122
  - use in MS therapy, 122
- IFN- $\gamma$ 
  - effects on oligodendrocytes, 122, 179
  - role in EAE and MS, 179
  - upregulation of chemokines, 179
- IGF
  - oligodendrocyte survival and differentiation, 164
  - OPC differentiation, 59
  - PNS neurotrophic factor, 46
  - production by oligodendrocytes, 17
  - proliferation of OPCs, 98
  - remyelination, 185
  - survival of Schwann cell precursors, 26
- IL-1 $\beta$ 
  - effect on OPCs, 121
  - expression in the CNS, 121
- IL-6
  - effect on neuron and oligodendrocyte survival, 121
  - effect on OPC differentiation, 121
- IL-18
  - expression by oligodendrocytes, 121
- immature oligodendrocytes
  - susceptibility to excitotoxicity, 191
- immature OPC
  - A2B5, 57
- immature Schwann cells, 27
  - autocrine survival loop, 27
  - role in radial sorting of axons, 27
- immune-mediated diseases affecting oligodendrocytes
  - multiple sclerosis, 115
- immune-privileged organ
  - CNS, 135
- integrins
  - expression by OPCs, 99
  - role in myelination, 99
- interferon- $\beta$ 1
  - multiple sclerosis
    - drug treatments, 117
- ionotropic glutamate receptors, 186,
- iron toxicity
  - damage to oligodendrocytes, 168
- ischemia
  - in PVL, 189
- JC-virus
  - cause of PML, 118
  - glial specificity, 118
- juxtaparanode, 34, 37, 80
  - Caspr2, 37, 81
  - molecular changes causing disease, 38
  - myelin mutants, 38
  - PNS, 38
  - potassium channels, 81
  - TAG-1, 37, 81
- kainate receptors
  - expression by oligodendrocytes, 191
- LIF
  - effects on oligodendrocytes, 123
  - prevention of oligodendrocyte apoptosis, 123
- LINGO-1, 62
  - as an inhibitor of myelination, 29
- lymphocytes, *see* CD3 CD4 and CD8 T cells
  - interaction with oligodendrocytes, 133
- macroglia, 2
- macrophages
  - activation by CD4<sup>+</sup> T cells, 132
  - in chronically demyelinated lesions, 174
  - in early MS lesions, 173
  - immunoglobulin deposits in MS, 178
  - interaction with oligodendrocytes, 132
  - PVL, 187
  - ROS, RNS, 181
- MAG, *see also* myelin proteins
  - as an adhesion molecule, 129
  - axonal regeneration in MAG knockouts, 41
  - domain specific targeting, 90
  - inhibition of neurite outgrowth, 39
  - loss in MS lesions, 179

- myelin associated inhibitor, 39
- myelination in MAG knockouts, 32
- promotion of neurite growth in
  - embryonic neurons, 40, 129
- receptors involved in mediating inhibition, 40
- role in axon regrowth in PNS, 47
- role in limiting axonal regeneration, 41
- role in PNS regeneration, 46
- S-MAG and L-MAG, 82
- structure, 82
- maternal intrauterine infection
  - PVL, 190
- maturation of OPCs
  - pro-oligodendrocytes, 57
- mature oligodendrocytes
  - antigenic markers, 187
  - capacity for remyelination, 140
  - capacity for remyelination after transplant, 140
  - susceptibility to excitotoxicity, 191
- MBP
  - compaction of myelin, 33
  - effects of mutations, 73
  - functions, 72
  - GOLLI gene structure, 72
  - involvement in myelin spiraling, 73
  - localization by mRNA
    - translocation, 92
  - MBP-deficient mice, 34
  - shiverer mice, 34
  - shiverer mice and rats, 73
- membrane attack complex
  - in EAE, 178
- mesenchymal or stromal stem
  - cells. *see* bone-marrow-derived stem cells
- metabotropic glutamate receptors, 186
  - expression in white matter, 195
  - neurons, 195
- MHC class I
  - expression by oligodendrocytes, 120, 177
- MHC class II
  - expression by oligodendrocytes, 120, 177
  - induction of expression by oligodendrocytes, 120, 177
- microarray technology
  - use in developmental studies, 105
- microglia, 2, 133
  - activated, 133
  - expression of FasL in MS lesions, 133
  - interactions with oligodendrocytes, 133
  - ROS, 182
- microRNAome. *see* miRNAs
- microRNAs. *see* miRNAs
- microtubule network
  - during oligodendrocyte differentiation, 86
  - enrichment of  $\beta$ IV tubulin, 87
  - molecular motors, 86
  - MT organizing center, 86
  - myelin dysfunction after disruption, 86
  - oligodendrocyte polarization, 86
  - taiep mutants, 86
  - tau, 88
- miRNAs
  - brain-enriched, 111
  - brain-specific, 111
  - expression during glial lineage progression, 112
  - glioblastoma, 112
  - mechanism of action, 110
  - neuropathological conditions, 112
  - oligodendrocyte genes targeted by, 113
    - galactocerebrosidase (GALC), 113
    - MBP, 113
  - role in Alzheimer disease, 112
  - role in brain homeostasis, 111
  - role in human neural diseases, 112
  - role in schizophrenia, 112, 113
- mitoxantrone
  - multiple sclerosis
    - drug treatments, 117
- MOG, 83
  - antibody response to native protein, 132
  - binding to complement, 130
  - cellular functions, 131
  - function, 83
  - induction of EAE in TNF- $\alpha$  knockouts, 122
  - in MS lesions, 180
  - role of anti-MOG antibodies in demyelination, 131
  - use in induction of EAE, 119, 131
- motor neuron progenitor (pMN) domain, 104
  - generation of oligodendrocytes, 22
- mRNA transport
  - localization of MBP, 92
- MS. *see* multiple sclerosis
- multiple sclerosis, 115, 171
  - axonal injury, 116, 135, 148, 149,
  - chronic disability, 148
  - drug treatments, 117
  - failure of myelin repair, 137
  - hallmarks of disease, 116
  - histopathological patterns, 116
  - NAWM, 148

- multiple sclerosis (cont.)
  - neuroanatomical structures
    - frequently affected, 117
  - pathology of chronic lesions, 174
- multiple sclerosis lesions
  - apoptosis of oligodendrocytes, 173
  - axonal injury, 117
  - complement activation, 130
  - dying-back oligodendroglialopathy, 174
  - early pathology, 173
  - glutamate-mediated mechanisms, 180
  - histopathological hallmarks, 171
  - immunoglobulin deposition, 178
  - initial signs of myelin degradation, 174
  - morphological signs of apoptosis, 174
  - patterns of oligodendroglial pathology, 173
  - periplaque white matter (PPWM), 173
  - perivascular inflammation, 116
  - reduction in OPCs over time, 184
  - similarity of early lesion to stroke, viral CNS disease, 180
  - TRAIL pathway, 175
- myelin
  - age-related changes, 12
  - compact, 4, 65
    - formation, 5
  - composition of plasma membranes, 69
  - concentric myelin, 8
  - differences between CNS and PNS, 19
  - in invertebrates, 8
  - increase in conduction velocity, 5
  - lipid composition, 69
  - modulation of thickness, 98
  - myelination of frontal lobes, 12
  - myelin-specific components of
    - Schwann cells and oligodendrocytes, 33
  - non-compact, 4, 66
    - axo-glial junction, 5
    - formation of, 5
  - pathology in spinal cord injury, 154
  - pathology in the aging CNS, 168
  - proteins, 70
  - role in learning complex skills, 12
- myelin basic protein. *see* MBP
- myelin gene mutations
  - galactocerebrosidase (GALC), 109
  - PLP, 108
- myelin inhibitors of axonal regeneration
  - ephrin-B3, 42
  - netrin-1, 42
  - Nogo, MAG, 39
  - repulsive guidance molecule A, 43
  - Sema4D, 43
  - stabilization of CNS circuitry, 43
- myelin model, 12
- myelin proteins, *see also* MAG
  - CD9, 74
  - claudin-11, 75
  - CNP, 76
  - DM20, 71
  - domain-specific targeting, 89
  - MAG, 23, 29, 32, 34, 39
  - MAL, VIP17/MVP17, 73
  - MBP, 23, 28, 33, 72, 108, 119, 124, 131, 173, 176, 179, 188, 195
  - MOG, 83, 119, 122, 130, 173, 180
  - myelin-oligodendrocyte basic proteins (MOBPs), 73
  - P0, 19, 28, 32, 33, 34, P2, 73
  - PLP, 19, 23, 25, 33, 58, 71, 108, 124, 150, 173, 176, 179
  - PLP/DM20, 33
  - PMP22, 19, 25, 34
  - secretory pathway, 89
- myelin repair, 137 *see* remyelination
  - Schwann cells, 142
  - therapeutic, 145
- myelin thickness
  - regulation of, 31
- myelination
  - axonal control, 28
  - axonal determination of myelin thickness, 96
  - axonal signaling, 97
  - control of onset, 62
    - axon size, 62
  - evolution, 8
  - in third and fourth decade, 64
  - integrins, 99
  - internodes, 4
  - mechanisms in the CNS, 63, 84
  - microtubule network, 84
  - molecular mechanisms, 84
  - role of adhesion molecules; L1; NCAM, 31
  - number of internodal segments, 4, 65
  - number of processes, 65
  - regulation of axon caliber, 100
  - relationship between
    - oligodendrocytes and axons, 96
    - role of cell-to-cell contact, 31
- myelin-related genes
  - dysregulation in psychiatric disorders, 10

- Na<sup>+</sup>/K<sup>+</sup> ATPases, 82
- natalizumab
  - multiple sclerosis
    - drug treatments, 117
- nerve growth factor (NGF)
  - affect on myelination, 29
- nerve injury
  - myelin clearance, 44
- nerve regeneration
  - PNS, 47
- neural injury
  - impact of Schwann cells, 43
- neural tube, 50
  - earliest detectable OPCs, 51
  - stem cells, 50
- neuregulin-1
  - activation by BACE1, 98
  - ErbB receptors, 97
  - role in ensheathment and myelination in the PNS, 31
  - role in Schwann cell development, 30
  - signaling during myelination, 97
  - survival of Schwann cell precursors, 25
- neurofascins
  - neurofascin 186, 78
  - NF155, 80
  - role in Na<sup>+</sup> clustering, 36
- neurogenin
  - neurogenin-negative cells, 25
  - neurogenin-positive cells, 25
  - role in Schwann cell development, 25
- neuroglia
  - cells comprising, 1
  - derivation of the term, 1
  - description by Rudolph Virchow, 1
- neuromyelitis optica, 119
  - aquaporin-4 as a target antigen, 119
  - histopathology, 119
  - immunopathogenesis, 119
  - inflammatory infiltrates, 119
- neuronal regeneration
  - CNS vs PNS, 38
- neurons, 50
- neurospheres
  - stems cells, 50
  - use in therapeutic myelin repair, 147
- neurotrophic factor
  - secretion by oligodendrocytes, 150
- neurotrophic growth factors
  - BDNF, GDNF, IGF, NGF, 17
  - produced by oligodendrocytes, 17
- NF-κB
  - anti-apoptotic activity, 128
  - interaction with corticosteroids, 128
- NG2<sup>+</sup> cells
  - communication with neurons, 14
  - expression of NMDA receptors, 164
  - generation of action potentials, 15
  - at node of Ranvier 35, 36
  - nomenclature, 14
  - proliferation, 164
  - reaction after spinal cord injury, 163
  - role of glutamate and ATP in differentiation, 164
- NGF
  - opposing effects in PNS and CNS, 29
- NK cells
  - in EAE, 177
  - injury of oligodendrocytes, 177
- Nkx2.2
  - upregulation after SCI, 163
- NMDA receptors
  - blockers, 195
  - expression by NG2<sup>+</sup> cells, 164
  - expression by oligodendrocytes, 193
  - expression in white matter, 193
  - glutamate excitotoxicity, 194
- NMO
  - pathogenic antibody deposition, 119
- node of Ranvier, 34, 78
  - clustering of sodium channels, 35, 139
  - CNS, 35
  - contribution of glial cells to the formation of nodes, 34
  - ECM in the PNS, 35
  - flanking by paranodal loops, 36
  - generation of action potentials, 19
  - interaction with NG2<sup>+</sup> cells, 14
  - nodal microvilli, 35
  - PNS, 35
  - PNS vs CNS, 19
  - proteins, 78
  - stabilization by OMgp, 40
- Nogo
  - inhibition of axonal growth, 39
- non-compact myelin, 4, 5, 66, 75
  - abaxonal membrane, 66, 75, 83
  - adaxonal membrane, 66
  - CNP, 76
  - connexins, 77
  - cytoplasmic channels, 67
  - inner mesaxon, 66, 81
  - in invertebrates, 8
  - juxtaparanode, 80
  - MAG, 81
  - nodal region, 78



- non-compact myelin (cont.)
  - outer mesaxon, 66
  - outer tongue process, 83
  - paranodal loops, 66, 75, 79
  - periaxonal membrane, 75
- notochord, 53
- Nr-CAM, 78
- NRG1, *see* neuregulin-1
- O2A cells
  - oligodendrocyte type 2 astrocyte progenitors, 54
- olfactory ensheathing cells
  - use in therapeutic myelin repair, 146
- olig genes
  - regulation of cell fate, 56
  - roles during CNS development, 56
- olig1
  - genes essential for oligodendrocyte development, 55
  - specification of oligodendrocytes, 22
- olig2
  - expression by motoneurons, 56
  - PVL, 189
  - upregulation after SCI, 163
- oligodendrocyte development
  - transcription factors
    - Sox17, 105
- oligodendrocyte differentiation
  - differentially regulated genes, 105
  - epigenetic factors, 61
  - galactocerebroside (O1), 57
  - intrinsic timing mechanisms, 61
  - Notch signaling pathway, 29
  - transcription factor expression, 105
  - upregulation of transcription factors, 106
- oligodendrocyte induction
  - sonic hedgehog, 22
  - transcriptional control, 55
- oligodendrocyte precursor cells, *see also* oligodendrocyte progenitor cells
  - oligodendrocyte-type-2 astrocyte (O-2A), 23
  - role in remyelination, 141
- oligodendrocyte progenitor cells, *see also* NG2<sup>+</sup> cells
  - development
    - olig1 and olig 2, 55
    - transcription factors Nkx2.2 and Sox10, 56
  - developmental origin, 20
  - differentiation, 23, 84
    - intrinsic and extrinsic cues, 61
  - differentiation block in MS lesions, 185
  - dorsally derived, 22
  - formation of synapses, 13
  - inhibition by BMPs, 53
  - initial appearance in development, 53
  - migration during development, 4
  - NG2<sup>+</sup> cells, 13
  - origin of remyelinating progenitors, 142
  - origins, 51
  - remyelination, 184
  - role in spontaneous remyelination, 142
  - use in therapeutic myelin repair, 146
  - waves of migration during development, 57
- oligodendrocyte specification, 103
  - basic helix-loop-helix (bHLH) transcription factors, 103
  - bone morphogenic proteins (BMPs), 103
  - gradients of induction signals, 104
  - Nkx2.2, 104
  - sonic hedgehog (Shh), 103
- oligodendrocyte-myelin glycoprotein (OMgp)
  - inhibition of neurite outgrowth, 39
- oligodendrocytes
  - in the aging CNS, 167
  - antigenic markers during development, 57, 187
  - anti-inflammatory response, 16
  - apoptosis in MS lesions, 173
  - comparison with Schwann cells, 19
  - damage in disease, 138
  - discovery of, 2
  - expression of MAPs, 88
  - functions other than myelination, 11
  - immature, markers, 23
  - immune properties, 120
  - loss in MS lesions, 171
  - morphology, 3, 64, 65
  - multiple sources of, 23
  - myelin-specific components, 33
  - role in psychiatric disorders, 9
  - surface area of membrane, 4, 67
  - susceptibility to death receptor stimuli, 175
  - terminally differentiated, markers, 23
  - trophic effect on axons, 150
  - trophic support of axons, 150
- oligodendrogenesis
  - cre-lox fate mapping, 22
  - transcriptional control, 55
  - waves of migration, 104

- oligodendroglial injury
  - iron toxicity, 168
- oligodendroglial injury in MS, 174
  - antibody- and complement-mediated mechanisms, 178
  - apoptosis-related mechanisms, 174
  - cell-mediated mechanisms, 175
  - cytokine-mediated mechanisms, 179
  - glutamate-mediated mechanisms, 180
  - role of complement, 178
  - ROS- and RNS-mediated mechanisms, 181
- oligodendroglial injury in SCI, 158
  - cause of oligodendrocyte death, 158
- oligogenesis
  - in the adult CNS, 164
- OMgp
  - growth cone collapse, 40
- OPC migration
  - during development, 59
  - GABA(B) signaling, 60
  - netrin-1 as a chemorepellant, 60
  - PDGF, 59
  - regulation by Eph and ephrins, 59
  - stop signals, 60
  - tyrosine kinases, 60
  - WAVE proteins, 60
- OPC mitogens
  - FGF, 58
  - PDGFA, 58
- OPCs, *see also* oligodendrocyte progenitor cells
  - immature
    - expressing A2B5, 57
- P0, 70
  - functions, 34
- P2, 73
- paranodal loops, 79
  - gap junctions, 79
- paranode, 5, 34
  - adherens junctions, 37
  - Caspr, 37
  - contactin, 37
  - differences between CNS and PNS, 37
  - formation of diffusion barrier, 36
  - NF155, 37
  - paranodal loops, 66
- PDGF $\alpha$ 
  - mitogen for NG2<sup>+</sup> cells, 164
- Pelizaeus–Merzbacher disease, 138
- periventricular leukomalacia
  - premature birth, 186
  - glutamate excitotoxicity, 186
  - gray matter injury, 187
  - hypoxic ischemia, 189
  - maternal infection, 190
  - pathogenesis, 191
  - pathology, 187
  - white matter injury, 187
- peroxisomes
  - inactivation in oligodendrocytes, 11
- PLP, 101
  - domain-specific targeting, 90
  - effects of mutations, 71, 150
  - functions, 71
  - Jimmy mice, 92
  - Pelizaeus–Merzbacher disease, 33
  - PLP-deficient mice, 33
  - spastic paraplegia type 2, 33
- PML, *see* progressive multifocal leukoencephalopathy
- PMP22
  - Charcot–Marie–Tooth type 1A, 34
  - function, 34
- polydendrocytes, *see* NG2<sup>+</sup> cells
- post-transcriptional regulation of myelination, 110
  - microRNAs (miRNAs), 110
- premyelinating oligodendrocytes, 84
  - $\beta$ IV tubulin, 87
  - non-polarized membranes, 84
- pre-oligodendrocytes
  - antigenic markers, 188
  - susceptibility to excitotoxicity, 191
- progressive multifocal leukoencephalopathy
  - immune deficiencies, 118
  - injury to oligodendrocytes, 117
  - JC virus, 117
  - triggering by natalizumab therapy, 118
- pro-oligodendrocytes, 23
  - O4+, 57
- proteomic screening, 64
  - identification of target proteins, 9
- PSA-NCAM, 62
  - negative regulator of myelination, 30
- psychiatric disorders
  - role of oligodendrocytes in, 9
- PVL. *see* periventricular leukomalacia
- radial sorting of axons, 28
- reactive gliosis
  - secondary spinal cord injury, 155
- reactive nitrogen species, 181
- reactive oxygen species, 181
- remyelination
  - characteristics of remyelinated axons, 182
  - characteristics of repaired myelin, 139

- remyelination (cont.)
  - in chronic MS lesions, 183
  - cortical, 140
  - effect of the immune response on, 144
  - failure in chronic MS lesions, 185
  - failure to complete, 143
  - imaging, 147
  - impairment of OPC migration, 144
  - inhibitors in the MS lesion, 144
  - light microscopic hallmarks, 183
  - mature oligodendrocytes, 140
  - monitoring in patients, 147
  - in MS lesions, 182
  - oligodendrocyte progenitor cells, 184
  - OPC differentiation block, 144
  - protection of axons, 151
  - recovery from acute MS relapse, 137
  - role of antibodies in enhancing, 178
  - role of macrophages, 144
  - after SCI, 160
  - spontaneous, 139
  - spontaneous remyelination in MS, 139, 143
  - spontaneous repair by Schwann cells, 146
  - transplant of oligodendrocyte progenitors, 142
  - white vs gray matter, 184
- rituximab
  - multiple sclerosis drug treatments, 134
- Rudolph Virchow
  - description of neuroglia, 1
- Schmidt-Lanterman incisures, 34, 37, 68
- Schwann cell precursors
  - as cellular chaperons, 26,
  - markers, 25
  - role in nerve development, 26
  - as a source of endoneurial fibroblasts, 27
  - source of neurotrophic factors, 26
  - survival factors, 25
- Schwann cells, 68
  - achieving a 1 to 1 ratio with axons, 28
  - axonal determination of myelination, 31
  - basal lamina, 19
  - boundary capping cells, 24
  - contribution to CNS remyelination, 142
  - dedifferentiation after nerve injury, 44
  - development, 24, 25
  - developmental stages, 24
  - long-term denervation, 47
  - microvilli, 35
  - myelinating profile, 28
  - myelin-specific components, 33
  - origin, 24,
  - specification, 23
  - spontaneous remyelination in MS, 146
  - tumor formation after transplantation, 146
  - use in therapeutic myelin repair, 145,
- SCI, *see* spinal cord injury
- secondary demyelination
  - bystander oligodendrocyte damage, 138
- secretory pathway
  - unfolded protein response, 91
- shiverer mice, 34, 100
- single nucleotide polymorphisms (SNPs)
  - association with disease phenotype, 105
- sodium channel clustering
  - ankyring, 35
  - CNS, 36
  - Nav1.6, 78
  - NF186, 35
  - Nr-CAM, 35
  - role of Schwann cells, 36
  - tenascin-R, 36
- sonic hedgehog (Shh)
  - graded signaling in the notochord, 53
  - induction of Olig1 and Olig2, 22
  - involvement in OPC appearance during development, 53
- spinal cord injury, 154
  - cell proliferation, 163
  - contusion injury, 154
  - contusion models, 161
  - downregulation of myelin proteins, 159
  - electrophysiological impairment, 161
  - inflammatory response, 155
  - potassium channels, 161
  - primary damage, 155
  - secondary damage, 155,
  - sodium channels, 161
- spiral growth
  - oligodendrocyte plasma membrane, 94
  - role of actin, 94
- stem cells
  - adult, 151, 152
  - bone-marrow-derived, 147, 152, 153,

- cell therapy in MS, 151
- embryonic, 151
- endogenous neural stem cells, 142
- induced pluripotent cells, 151
- mesenchymal, 153
- neural, 152
- neurospheres, 50
- origin of cells of the nervous system, 50
- signals controlling fate, 53
- therapeutic potential, 137
- T cells, *see* CD3 CD4 CD8 T cells
  - in early MS lesions, 173
  - HERV-W, 135
  - orchestration of immune response, 133
- $\gamma/\delta$  T cells
  - in acute and chronic MS lesions, 177
  - lysis of oligodendrocytes, 134, 177
- TAG-1
  - expression at the juxtaparanode, 37
  - function, 81
- Tau
  - role in microtubule stabilization, 88
- tenascin-R
  - role in CNS Na<sup>+</sup> channel clustering, 36
- TGF- $\beta$ 
  - effects on oligodendrocytes, 122
  - inhibition of NO, 133
- therapeutic myelin repair
  - adult stem cells, 152
  - bone-marrow-derived stem cells, 152
  - effect of ongoing inflammation, 147
  - embryonic stem cells, 146, 151
  - mesenchymal or stromal cells, 152
  - neuroprotection, 151
  - olfactory ensheathing cells, 146
  - OPCs, 146
  - protection of axons, 151
  - Schwann cells, 145,
  - targeting lesion sites, 147
- TLR, *see* toll-like receptors
- TLR2, TLR3
  - expression by oligodendrocytes, 125
- TNF- $\alpha$ , 121, 128, , 133
  - as a mediator of CNS inflammation, 129
  - effects on oligodendrocytes, 122
  - involvement in oligodendroglial apoptosis, 122
  - role in EAE and MS, 122
- toll-like receptors
  - effects of activation, 125
  - expression by oligodendrocytes, 125
  - recognition of pathogen-associated molecular patterns, 125
  - specific effects on oligodendrocytes, 125
- TRAIL system
  - in MS, 174
  - in oligodendrocytes, 175
  - role in apoptosis in EAE, 175
- transcription factors, 56, 104, 105, 180
  - Nkx6.1, Nkx6.2, 22
  - Oct-6/SCIP/Brn2, Krox-20, 28
  - olig1, olig2, 22
  - oligodendrocyte induction, 55
- transgenic mouse models, 108
  - ablation of Notch1, 29
  - BACE1-null, 98
  - blockade of erb in oligodendrocytes, 10
  - Caspr-deficient, 80
  - claudin-11 null, 75
  - Cnp1-deficient, 11, 77
  - connexin deficiencies, 78
  - effects of lipid deficiencies on myelin, 69
  - expression of PSA-NCAM, 30
  - MAG-null mice, 82
  - NgR1, 42
  - NRG1/Erb signaling, 30
  - overexpression of Akt, 99
  - overexpression of IFN- $\gamma$ , 122
  - overexpression of IGF-1, 99
  - overexpression of LINGO-1, 30
  - overexpression of NRG1 type III, 31
  - PLP deficiency, 71
  - PLP-null, 101
  - selective inactivation of oligodendroglial functions, 10
  - shiverer*, MBP, 100
  - TNF-R1 and FAS inactivation in oligodendrocytes, 175
  - trophic support of axons by oligodendrocytes, 150
  - use in determining oligodendrocyte function, 10
- trans-Golgi network (TGN)
  - domain-specific targeting, 89
- $\beta$ -tubulins, 87
- Wallerian degeneration, 44, 45, 46, 47
  - secondary spinal cord injury, 158