Glia and demyelinating diseases

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Animal models of demyelination
- EAE (experimental autoimmune encephalomyelitis)
- Virus induced (e.g. SFV, TMEV, MHV)
- Toxin induced (e.g. cuprizone, LPC, ethidium bromide)

Autoantibodies in demyelination
- Neurofascin: CCPD, Guillan-Barré, MS, EAE
- Myelin components (e.g. gangliosides, glycoproteins): Guillan-Barré, EAE, MS
- Aquaporin 4: NMO

Demyelinating diseases
- MS (multiple sclerosis)
- ADEM (acute disseminated encephalomyelitis)
- AHI (acute haemorrhagic leucoencephalitis)
- CCPD (combined central & peripheral demyelination)
- Guillan-Barré syndrome (peripheral nerve demyelination)
- NMO (Neuromyelitis Optica)
- Viral demyelination: PML (progressive multifocal leukoencephalopathy) & SSPE (subacute sclerosing panencephalitis)

Antibody production Complement activation Osmification of antibody

Proinflammatory astrocyte response:
- Expression of pattern-recognition receptors (TLRs, PKR)
- Antigen presentation (MHC I & II, CD80 & CD86)
- Cytokine & chemokine production. Activation, extravasation & homing of auto-reactive T-cells, macrophages & T-cells
- Recruitment of microglia to lesions (ICAM-1, VCAM-1, IL-12, IL-23, CXCL10, MCP-1, SAVIES)

Antigen presentation
- Phagocytosis of myelin debris & apoptotic cells
- Cytokine & chemokine production

Synapse homeostasis, stimulation of synaptic transmission (“tripartite synapse”)

Structure of oligodendrocyte (OPC)

Permeabilization of antibody

- Perforin release (causing axonal damage)

Axon injury

Promotion of remyelination

OPCs proliferate and migrate to demyelinated lesion

Astrocytosis

Protective astrocyte response:
- Limitation of T-cell-mediated inflammation (IL-4, IL-5, TLR3, IL-10, CTLA4)
- Production of neuroprotective molecules (NT-4, BDNF, CNTF, and LIF)

Production of "glial scar":
- Increased GFAP, nestin, vimentin
- May inhibit axon re-growth & migration of OPCs

Microglial activation signal

Microglia:
- Carry out immune surveillance in CNS
- Chemokine & cytokine production & phagocytosis of dead cells
- Release of glutamate, ATP, cytokines & growth factors
- Have interaction with neurons during development and neurogenesis
- Exist in 3 distinct morphologies: "ramified", "activated" and "phagocytic" (amoeboid)

M1 microglia
(M1OS, CD16/32, iNOS, CD14, CCL2, CXCL5, IL-12, IL-23, IL-1α, IL-1β, TNFα)

M2 microglia
(arginine-1, mannose receptor, IL-1R, TGFβ)

Activation signal

Retraction of branches

Axon

Myelin sheath

Protection of axons

Astrocyte

Pericyte

Endothelial cell

Microglial activation

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