

*The observation that MOG-deficient mice develop normally, without detectable neurological abnormalities – neither anatomical nor functional – raises questions for the physiological role of MOG in the healthy CNS. The fact that MOG has been strongly conserved in mammalian evolution suggests an important role in brain function. Indeed, we found that the N-linked glycan that is attached to the asparagine residue at position 32 is a ligand for the C-type lectin receptor DC-SIGN (Garcia-Vallejo et al., 2014). DC-SIGN is well known for its regulatory role in dendritic cell (DC) maturation, but the molecule is also expressed on CNS microglia (Garcia-Vallejo et al., 2014) and on myelin containing phagocytic cells in the brain-draining cervical lymph nodes (de Vos et al., 2002). Ligand binding to DC-SIGN antagonizes DC activation/maturation signals relayed via Toll-like receptors and keeps DC in a tolerogenic/anti-inflammatory state (Van Kooyk and Geijtenbeek, 2003). Microorganisms such as HIV or mycobacteria have high-jacked this function for immune escape (reviewed in Geijtenbeek et al., 2004). Intriguingly, pathogenic conditions (inflammation for example) can change the normal glycosylation of MOG (Garcia-Vallejo et al., 2014). These findings underlie the concept that MOG has a homeostatic role in the brain, which is lost under neuroinflammatory conditions. Conceptually, disturbance of this function, e.g. by structural modification of the N-linked glycan, is only noticed when the CNS is challenged, by infection (releasing PAMPS) or neurodegeneration (releasing DAMPS) for example, as the capacity to restore homeostasis after clearance of the challenge is disturbed (’t Hart and van Kooyk, 2004).*