Siglec-11 and Siglec-16

Description

As with Siglec-5 and Siglec-14, Siglec-11 and Siglec-16 form a pair of receptors with opposing functions: Siglec-11 is an inhibitory receptor while Siglec-16 is an activating one. They are both expressed in tissue macrophages and microglia. The expression of Siglec-11 on brain microglia is specific to humans. (Angata et al., 2002; Cao et al., 2008b) The nonfunctional Siglec-16P allele converted human Siglec-11, and the converted Siglec-11 allele became fixed in humans. As a result of this series of gene conversions, the extracellular portion of Siglec-11 and Siglec-16 is very similar. Consequently, they have maintained the same preferences in ligand binding, particularly towards Î±2-8-linked sialic acid oligomers and polymers (polySia).(Angata et al., 2002; Shahraz et al., 2015; X. Wang et al., 2012)

The roles in neurological disorders are still not clear. Siglec-11 interacts with polysialic acid in the brain, involved in diseases like schizophrenia, autism, and bipolar disorder. (Siddiqui et al., 2019) Studies revealed a neuroprotective function, reduced microglial phagocytosis of apoptotic neuronal material, and microglial neurotoxicity. (Y. Wang & Neumann, 2010) As a counterpart, the DAP12-associated activating receptor Siglec-16 activates the microglial phagocytic activity and proinflammatory signals. A perfect balance between these two signals is essential to maintain brain tissue homeostasis. It eliminates extracellular aggregates without causing inflammation. An impaired activity could otherwise lead to neuroinflammation and neurodegeneration. (Linnartz et al., 2010)

Structural information about these two proteins and the identification of possible ligands are still missing.

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