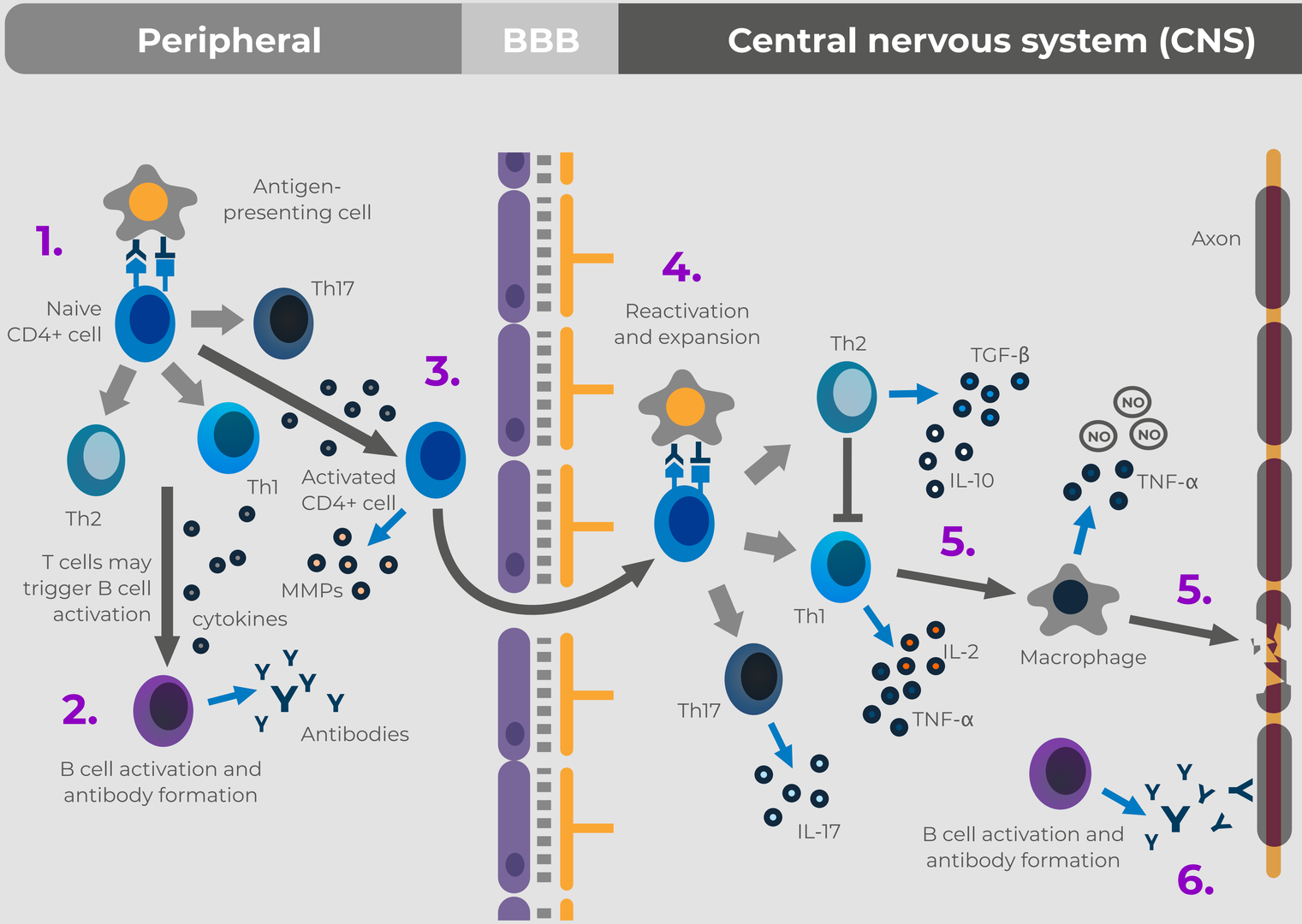
Simplified illustration of the immunopathogenesis of MS[1–5]



1 Naïve T cells bearing the CD4+ surface marker are activated by antigen-presenting cells and may differentiate into effector subsets including Th1, Th2 and Th17 (3).

2 Pro-inflammatory cytokines from Th1 and Th17 cells stimulate the activation and proliferation of B cells (3).

3 Activated T cells secrete pro-inflammatory cytokines that enable them to bind to the blood-brain barrier (BBB) (3). These bound T cells secrete matrix metallo-proteinases (MMPs) that compromise the BBB, thereby allowing activated T cells to enter the central nervous system (CNS) (1).

4 In the CNS, activated cells are reactivated by antigen presentation. T cells bearing the CD4+ surface marker may differentiate into Th1, Th2 and Th17 cells (3).

5 Reactivated T cells release pro-inflammatory cytokines such as IL-2 and TNF-α (7) and activate macrophages to enhanced phagocytic activity, production of cytokines such as TNF-α and the release of NO propagating demyelination and axonal loss (1).

6 Antibodies crossing the BBB or locally produced by activated B cells contribute to the destruction of the myelin sheath by antibody-mediated demyelination that involves complement activation (1).

1. Wiendl H and Kieseier B, Expert Opin Investig Drugs 2003 Apr; 12(4): 689-712. 2. Madsen C, Brain Behav 2017;7(6):e00696. doi: 10.1002/brb3.696. 3. Kieseier B, CNS Drugs 2011; 25 (6): 491-502. 4. Kasper L and Reder A, Ann Clin Transl Neurol 2014; 1(8): 622-631. 5. https://de.wikipedia.org/wiki/T-Helferzelle.
NO = nitric oxide; **IL**= interleukin; **TNF**-α = tumor necrosis factor α; **TGF**-β = transforming growth factor β

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