# Simplified Map of NMOSD/MOGAD

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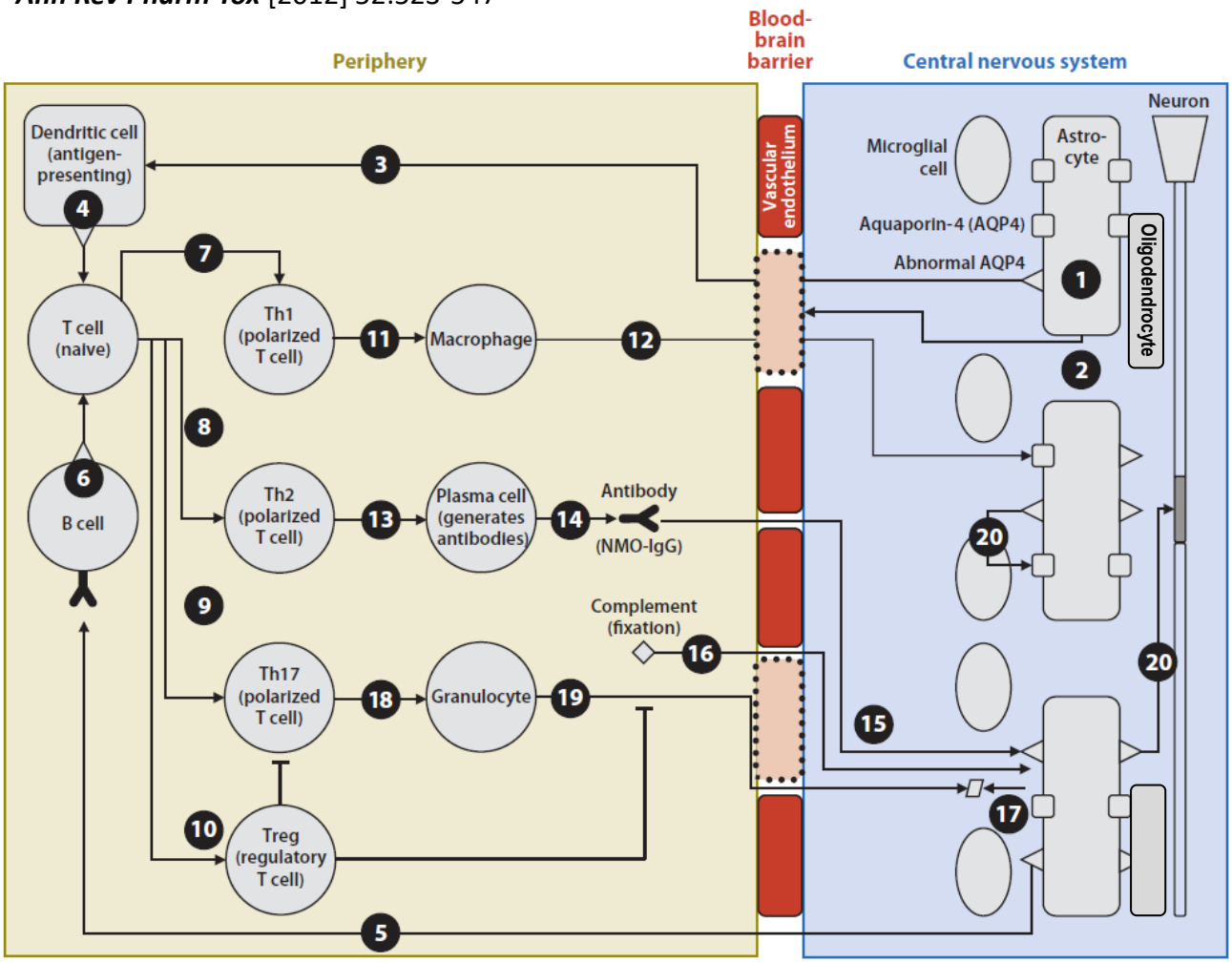


**Figure 5**

Hypothesized molecular and cellular determinants in neuromyelitis optica (NMO). Each number represents an immunologic component or event hypothesized to contribute to NMO: **1**, change in aquaporin-4 (AQP4) structure; **2**, altered astrocyte signaling [e.g., tumor necrosis factor (TNF), interleukin-6 (IL-6)]; **3**, detection and processing of abnormal AQP4 by dendritic cells [antigen-presenting cells (APCs)]; **4**, presentation of abnormal AQP4 epitopes to naive T cells; **5**, clonal selection of naive B cells by recognition of abnormal AQP4 epitopes; **6**, B cells may serve as APCs to present abnormal AQP4 to naive T cells; **7**, Th1 polarization of T cells (e.g., IL-12 context leading to interferon-$\gamma$ production); **8**, Th2 polarization of T cells (e.g., IL-4 and IL-13 context); **9**, Th17 polarization of T cells (e.g., IL-6, TNF, and transforming growth factor-$\beta$ context for induction of IL-17-producing T cells and generation of IL-22 and IL-23); **10**, failure of regulatory T cells (Tregs) to modulate autoreactive T and B cells; **11**, activation of Th1 effector cells such as macrophages; **12**, inflammation due to Th1 effector cells; **13**, activation of Th2 effector cells, such as plasma cells; **14**, autoantibody production (e.g., NMO-IgG); **15**, autoantibody targeting of abnormal AQP4 on astrocytes; **16**, complement fixation on bound autoantibody; **17**, cleavage of complement proteins creates inflammatory stimuli (e.g., C5a); **18**, activation of Th17 effector cells, such as granulocytes; **19**, infiltration of granulocytes into the central nervous system, which drives inflammation; **20**, possible antigen spreading, which promotes reactivity against other central nervous system components (e.g., myelin) and causes inflammatory demyelination and interference in neuroconductivity. (See also the **Supplemental Visualizing NMO tool**; follow the **Supplemental Materials link** from the Annual Reviews home page at **http://www.annualreviews.org**.)

Notes: