In patients with progressive MS, CNS-resident cells may predominantly fuel injurious processes. However, it remains unclear how immune responses are propagated and regulated within the CNS tissue. Examining the dynamics of immune cell accumulation in the CNS during Experimental Autoimmune Encephalitis (EAE), an animal model of MS, we found that T helper 17 cells induced robust collections of leukocytes within the brain meninges that were associated with local demyelination. An intricate network of stromal cells supported these meningeal aggregates that became dominated by B-lineage cells as disease progressed. Since agents that target B-lineage cells can have beneficial (rituximab, ocrelizumab) and detrimental (atacicept) effects in MS, we next examined specific CNS-resident B cell subsets. We focused on plasmablasts and plasma cells (PB/PC) since the originating source of PB/PC that appear in the inflamed CNS, and the role these cells play in disease pathogenesis, are unclear. Using reporter mice, we found that PB/PC are absent from the CNS during the steady-state but gradually increase in the brain and spinal cord during EAE. Notably, a portion of CNS-resident PB/PC were IgA+, and IgA+ PB/PC were found to be concomitantly decreased in the small intestinal lamina propria during the chronic phase of EAE. Using a series of approaches, we found that IgA+ B cells primed in the gut could be mobilized out of the intestine into extra-intestinal sites including the bone marrow, the lung, and the inflamed CNS. Removal of Blimp-dependent PB/PC resulted in exacerbated EAE that was normalized by the introduction of gut-derived IgA+ PC, and mice with an over-abundance of IgA+ PB/PC were resistant to EAE. These data generate new information regarding the source and function of CNS-resident B cells during neuroinflammation.

Note:
Prèire d’avisser vos étudiants gradués et stagiaires postdoctoraux afin d’avoir la participation de tous.