**Immunity in the Brain**

Until recently, the central nervous system (CNS) was thought to be cordoned off from the peripheral immune system, reliant only on its resident immune cells called microglia. Peripheral immune-cell breaches anywhere in the CNS were considered signs of disease. But researchers now know that diverse immune cells—possibly by the millions—circulate in the cerebral spinal fluid (CSF) and live in the brain's outer membranes even in healthy individuals.

**In Sickness and In Health**

The immune system is a critical part of a functioning central nervous system (CNS), even in the absence of injury. But most immune cells are largely relegated to the cerebral spinal fluid (CSF), the brain's meninges, and the epithelium of the choroid plexus. When the CNS experiences a major insult, however, immune cells join microglia in the parenchyma.

**Meninges**

- **Healthy Brain**
  - CD4+ T cells release IL-4
  - Neutrophils and macrophages migrate to the edge of the meninges, but don't enter the parenchyma. Macrophages clear dead cell debris. Neutrophils are also helpful for resolving injury, though it's not yet clear how. Microglia fill in spaces left by damaged or dead astrocytes to seal a leaky blood-brain barrier.

- **After Brain Injury**
  - D4+ T cells in the meningeal lining produce IL-4 cytokine, which prevents nearby macrophages from making proinflammatory molecules. If left unchecked, such proinflammatory signaling blocks a protein that astrocytes in the parenchyma need to support learning and memory.

**Choroid Plexus**

- **Alzheimer’s Brain**
  - Immunosuppressive signals from far off regulatory T cells (Tregs) reduce IFNγ signaling. This blocks normal trafficking of monocyte and CD4+ T cells from the blood and stroma to the cerebral-spinal fluid (CSF).

- **After Spinal Cord Injury**
  - Memory T cells ramp up production of IFNγ, which facilitates the migration of CD4+ helper T cells and monocytes from the blood and stroma into the CSF-filled ventricle, where they can access the site of injury.