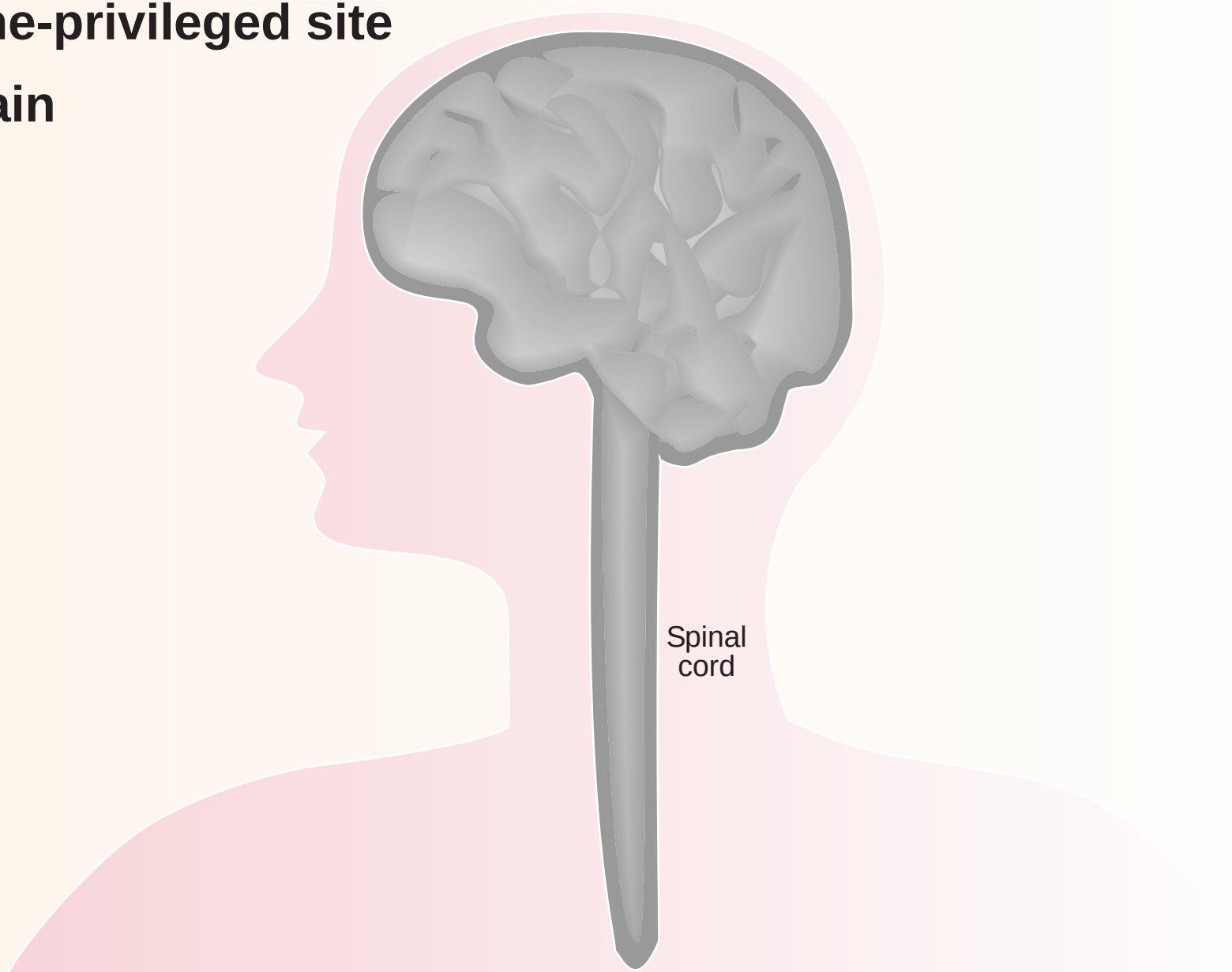
Immune-privileged site

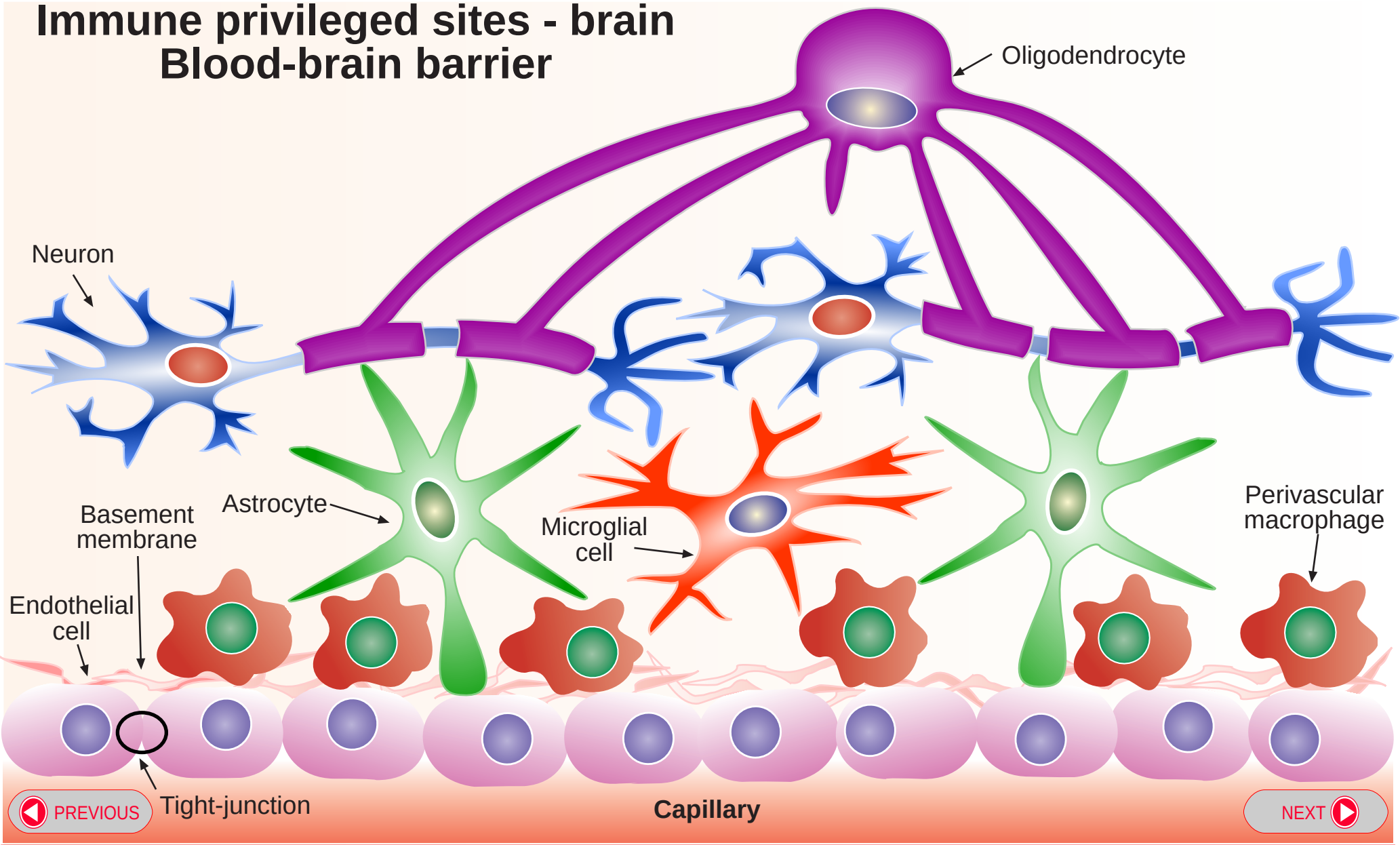
the brain



NEXT

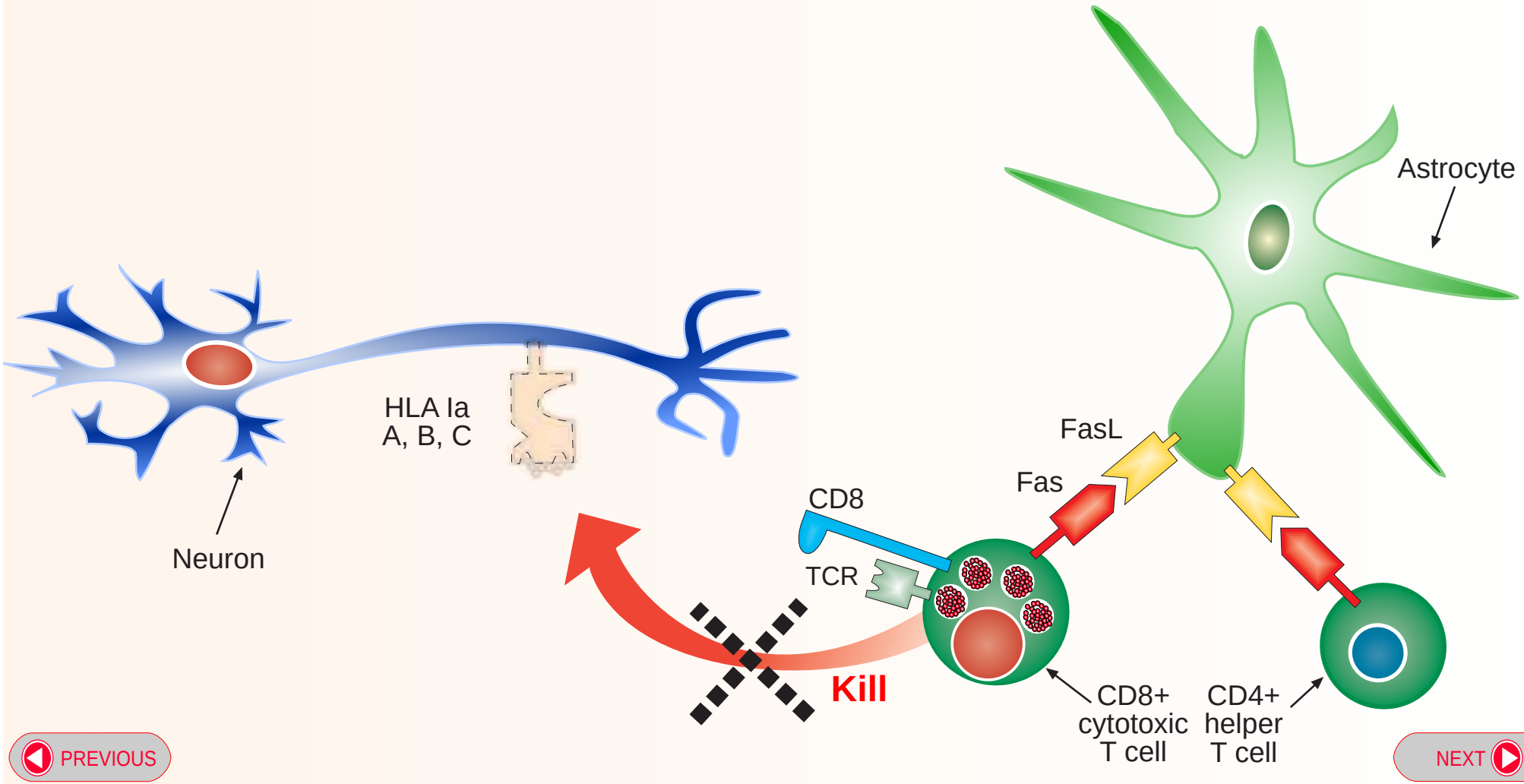
Immune privileged sites include the eye, brain, placenta and testis and are so-called because of mechanisms of immune-tolerance that operate to protect the tissues from immune-mediated damage. The central nervous system comprising the brain and spinal cord is an essential organ for survival, hence a balance between defense from pathogens and damage caused by inflammatory responses is needed. Activated immune cells secrete molecules that are neurotoxic and the encasement of the brain in the skull does not permit excessive infiltration of immune cells. Physiological barriers that control antigens and immune cell movement and additional mechanisms to regulate T cell responses are in place.

Immune privileged sites - brain
Blood-brain barrier



Neurons are highly susceptible to damage by inflammatory responses and have limited ability to regenerate. Oligodendrocytes and astrocytes can also be damaged and these cells are required for neuron function. Segregation of antigens from immune cells in the periphery is partially achieved by the blood-brain barrier. Capillary endothelial cells are connected by impermeable tight-junctions and there is a basement membrane that prevents soluble molecules from diffusing out of the brain. Since the brain lacks a lymphatic system, antigens drain to cervical lymph nodes along perivascular spaces or through ventricles into the CSF. Immune responses occur in the periphery and activated cells travel to the brain.

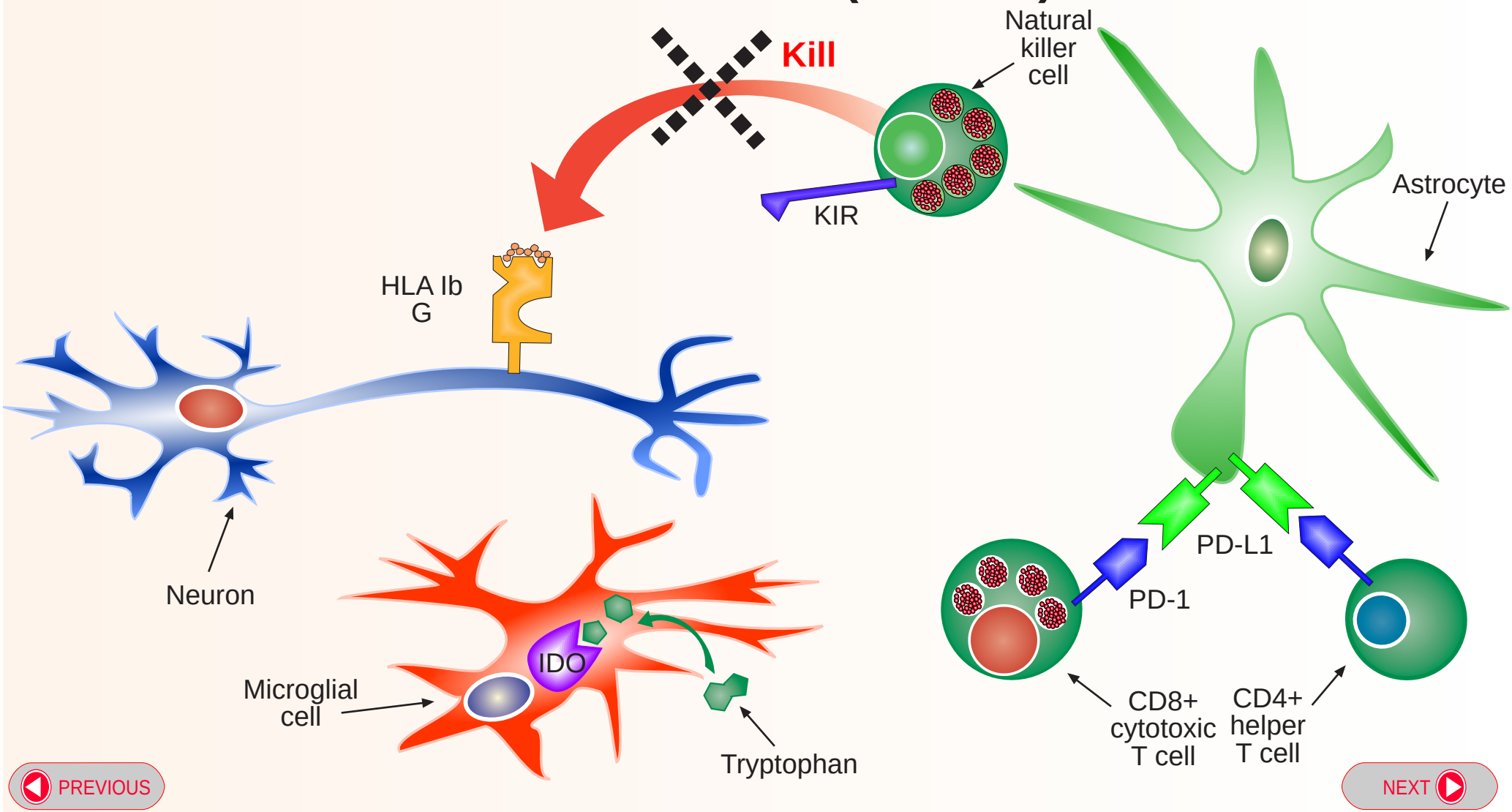
Immune privileged sites - brain
Immune evasion (constitutive)



PREVIOUS
NEXT

Immunoregulatory mechanisms in the brain circumvent damage to neurons and supporting cells such as oligodendrocytes and astrocytes. Mechanisms known to operate in the protection of neurons from attack by CD8+ cytotoxic T cells involve lack of expression of HLA class Ia A, B and C receptors. Astrocytes express cell surface FasL which promotes apoptosis in activated T cells by engagement with Fas.

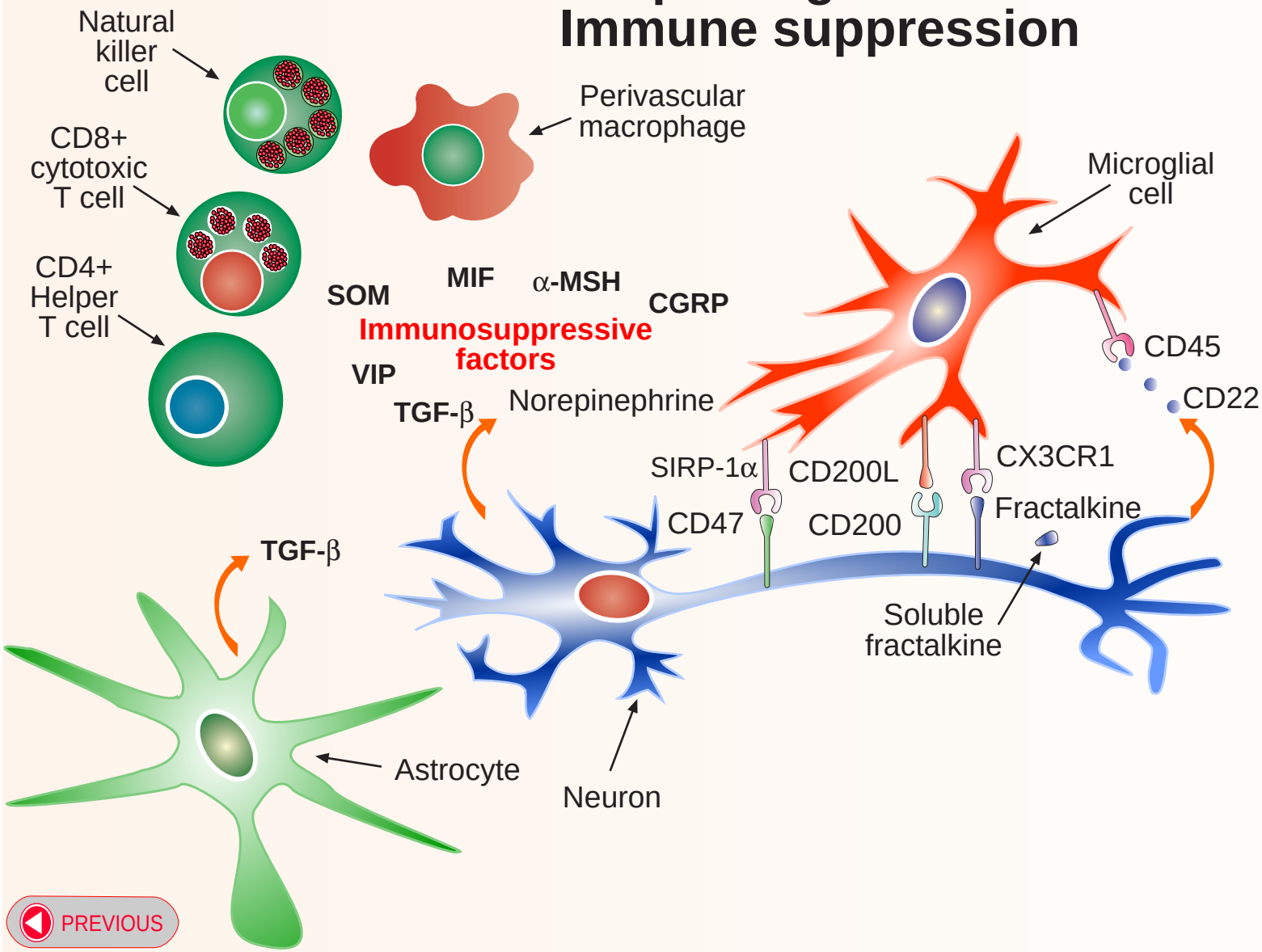
Immune privileged sites - brain
Immune evasion (induced)



PREVIOUS
NEXT

In brain inflammation, other immunoregulatory mechanisms are induced to reduce excessive pro-inflammatory responses that may damage neurons and supporting cells such as oligodendrocytes and astrocytes. Mechanisms known to operate in the protection of neurons from attack by natural killer cells is the induced expression of HLA class Ib G receptors that bind to NK inhibitory receptors such as KIR. Astrocytes upregulate surface PD-L1 receptors which promotes apoptosis in activated T cells by engagement of PD-1 receptors. In addition, microglial cells inhibit T cell proliferation by mediating depletion of tryptophan with IDO (indolamine 2,3-dioxygenase).

Immune privileged sites - brain
Immune suppression



PREVIOUS

NEXT

Throughout the central nervous system, neurons suppress activation of microglial cells by expression of cell surface receptors (eg. CD47, CD200 and fractalkine) that interact with ligands on microglial cells (SIRP-1α, CD200L and CX3CR1). Neurons also secrete soluble factors that regulate activation of microglial cells (CD22 and soluble fractalkine). A range of additional immunosuppressive factors secreted by neurons act on T cells, NK cells and macrophages. Both neurons and astrocytes secrete TGF-β, a powerful suppressor of activation of T cells, NK cells and macrophages.

List of abbreviations

SOM	Somatostatin
α–MSH	α–Melanocyte stimulating hormone
TGF-β	Tumour growth factor-beta
MIF	Macrophage migration inhibitory factor
CGRP	Calcitonin gene-related peptide
VIP	Vasoactive intestinal peptide
SIRP-1α	Signal regulatory protein 1-alpha
IDO	Indolamine 2,3-dioxygenase
KIR	Killer cell immunoglobulin-like receptor