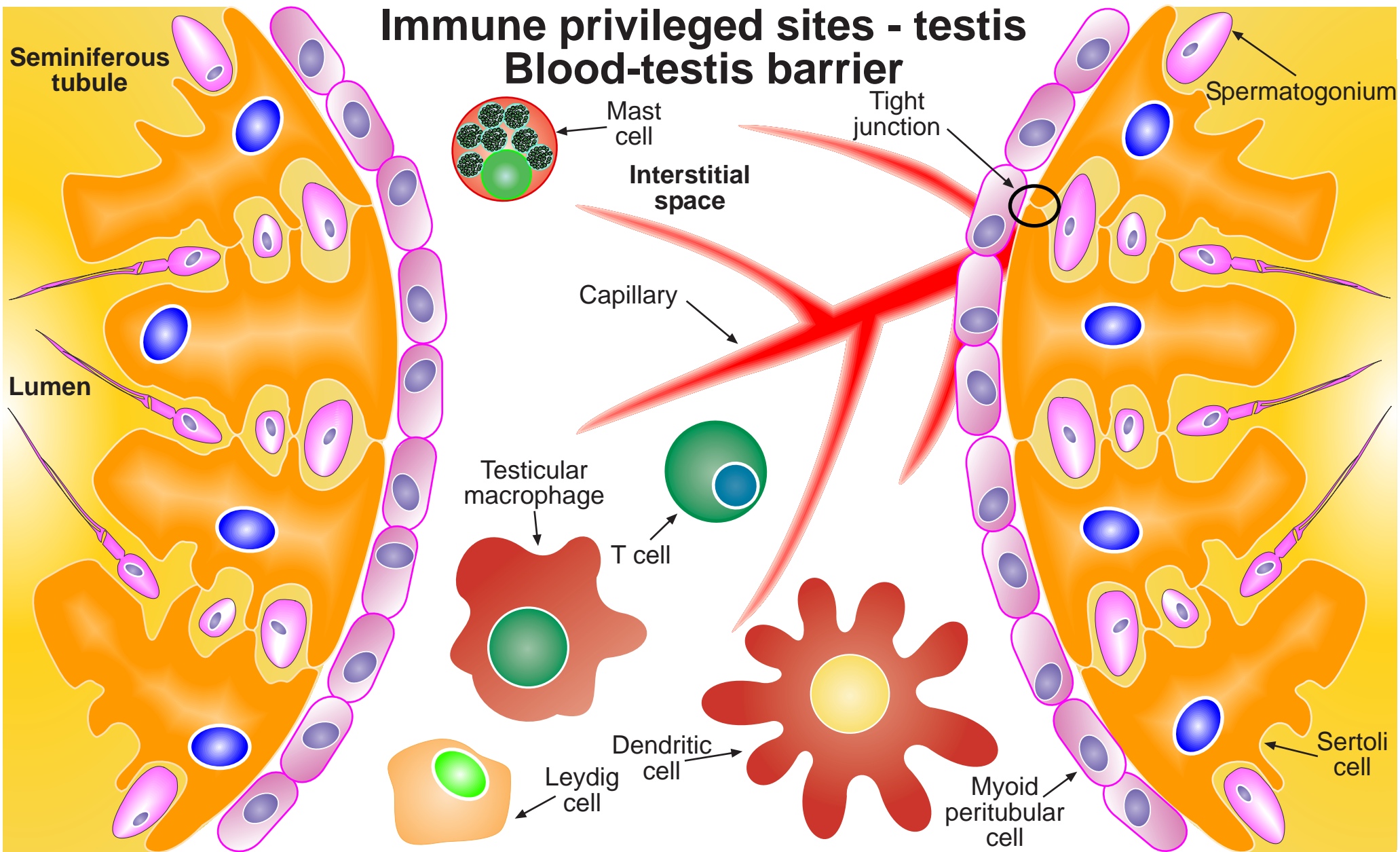


Immune privileged sites - testis

Blood-testis barrier

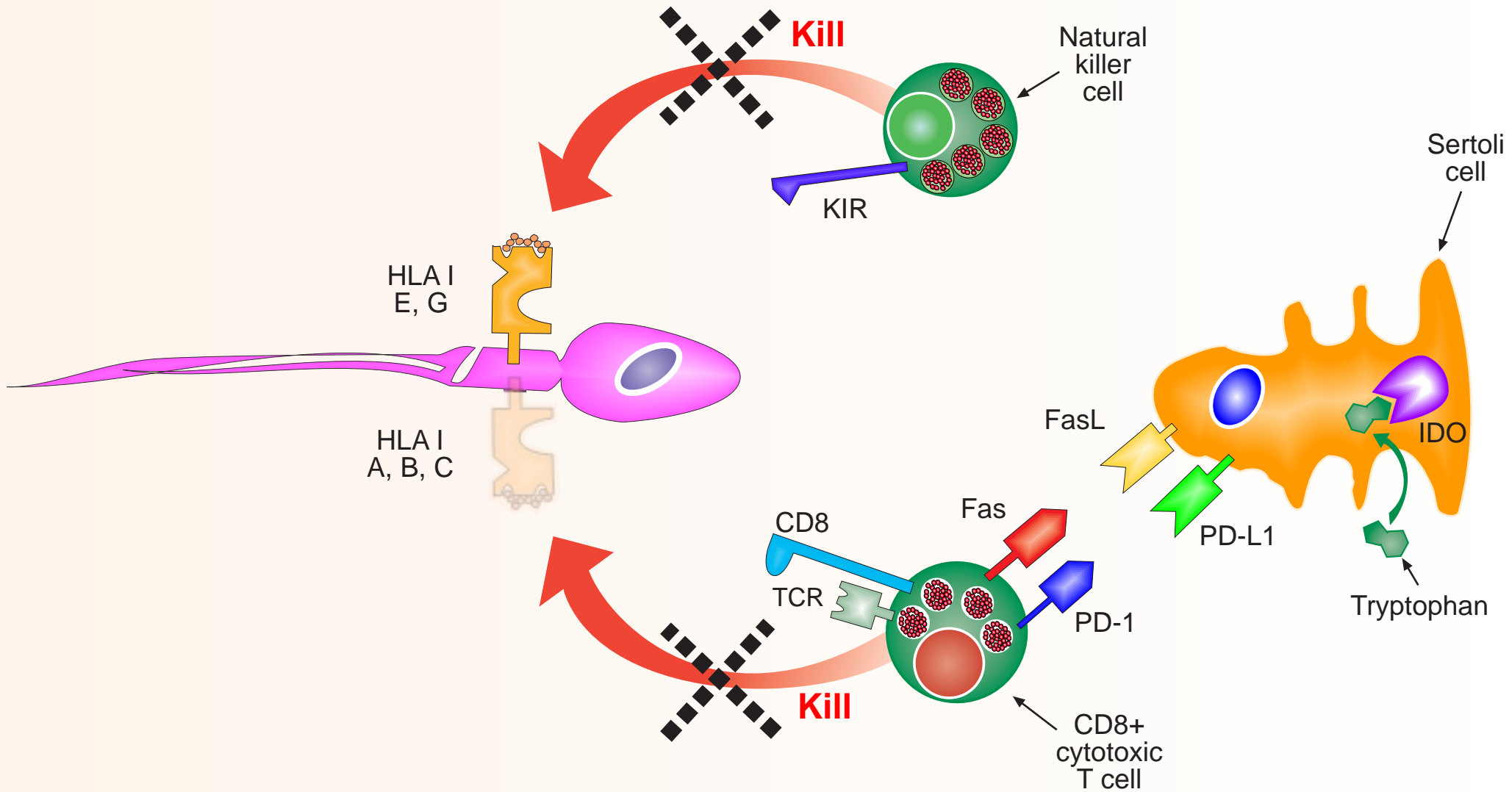


Immune privileged sites include the eye, brain, placenta and testis and are so-called because of mechanisms of immune-tolerance that operate to protect the tissues from immune-mediated damage. In the testis at the onset of puberty, new antigens are expressed during spermatogenesis and risk provoking an immune response. Segregation of antigens in the seminiferous tubules from immune cells in the interstitial space is achieved by a layer of Sertoli cells connected by impermeable tight junctions forming a blood-testis barrier. However, the barrier is incomplete such as in the rete testis and other mechanisms are therefore involved in active suppression of pro-inflammatory immune responses.



Immune privileged sites - testis

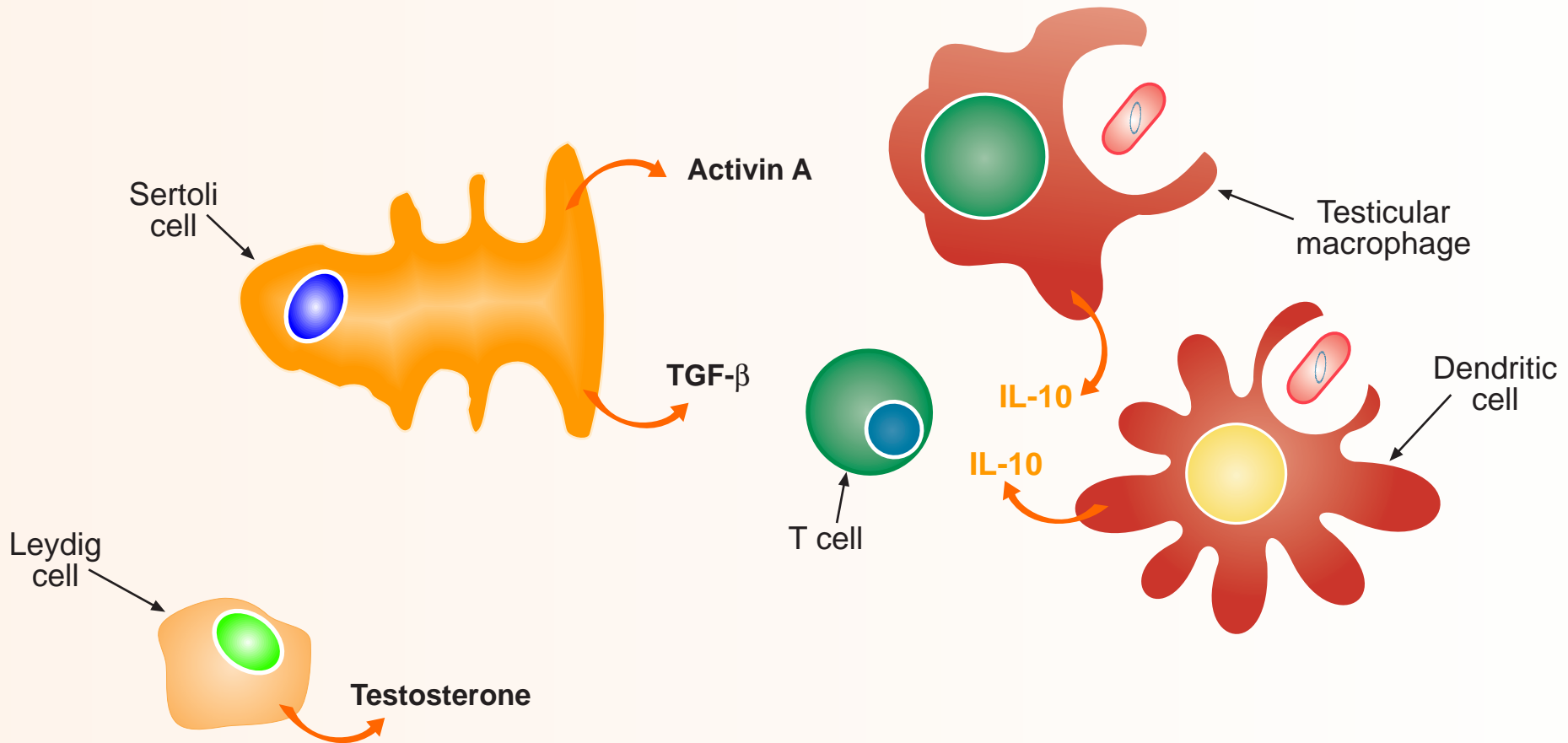
Immune evasion



The primary goal of immuno-suppressive mechanisms in the testis is to circumvent damage to cells or disruption of sperm production. Mechanisms known to operate in the protection of sperm cells from attack by cytotoxic immune cells such as natural killer cells and CD8+ cytotoxic T cells involve lack of expression class I HLA A, B and C receptors and the induced expression of class I HLA E and G receptors. Sertoli cells express cell surface ligands FasL and PD-L1 which promote apoptosis in activated T cells following engagement with respective Fas and PD-1 receptors. In addition, Sertoli cells inhibit T cell proliferation by mediating depletion of tryptophan with IDO (indolamine 2,3-dioxygenase).

Immune privileged sites - testis

Immune deviation



In the testis, cytokine production following activation of antigen presenting cells such as macrophages is skewed towards a “Th2-like” immunoregulatory/immunosuppressive profile. Activated macrophages produce IL-10 and very little IL-12. IL-12 is required to stimulate T-cells to differentiate into pro-inflammatory Th1 IFN- γ and IL-2 secreting cells that provide help to CD8+ cytotoxic T cells. Sertoli cells secrete Activin A that inhibits activated macrophages from producing pro-inflammatory cytokines such as IL-6 and TNF- α . Sertoli cells also secrete TGF- β that inhibits activated T cells from differentiating into cells with a Th1 phenotype. Finally, Leydig cells produce large quantities of testosterone which also has immunosuppressive properties.