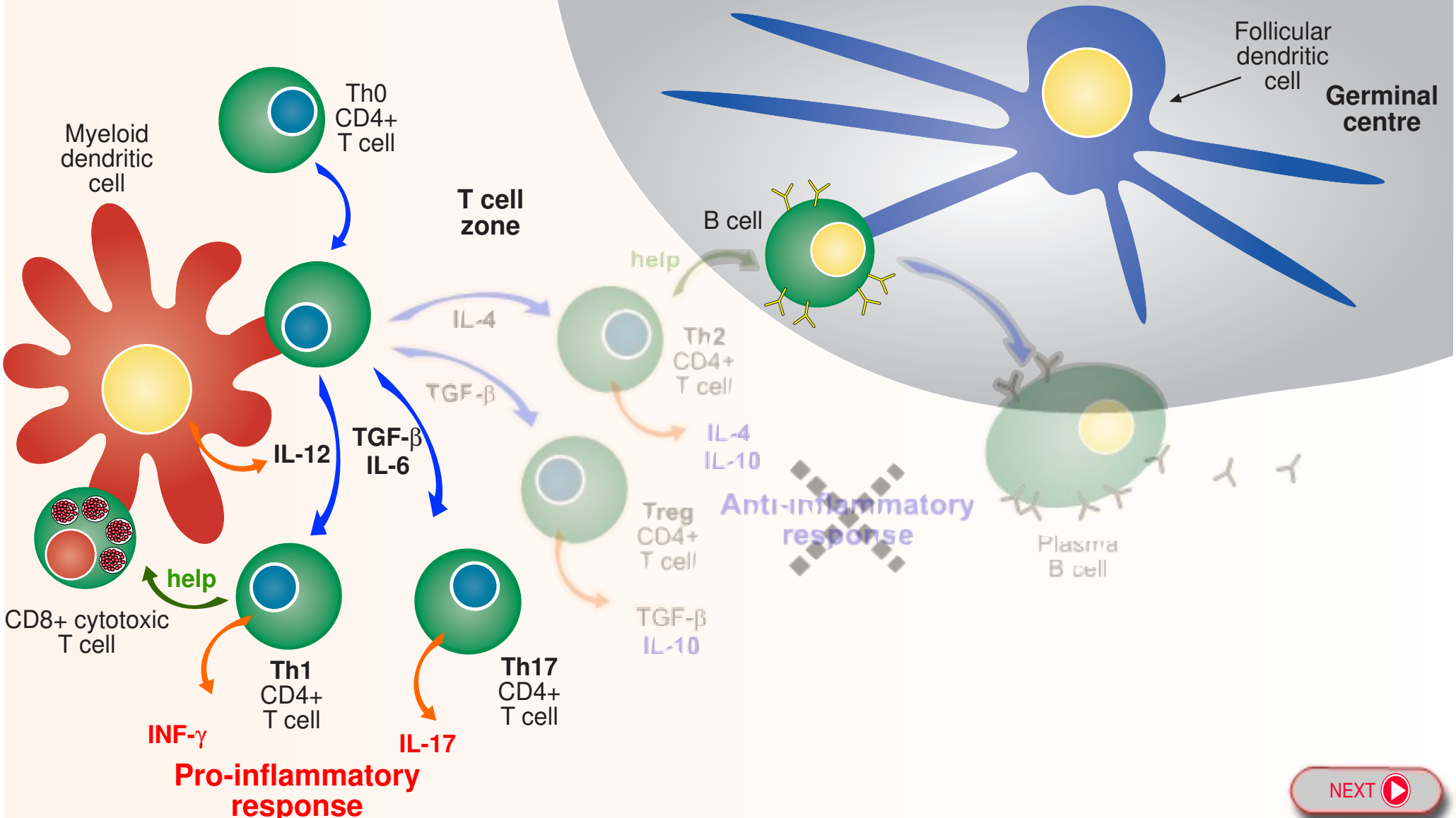
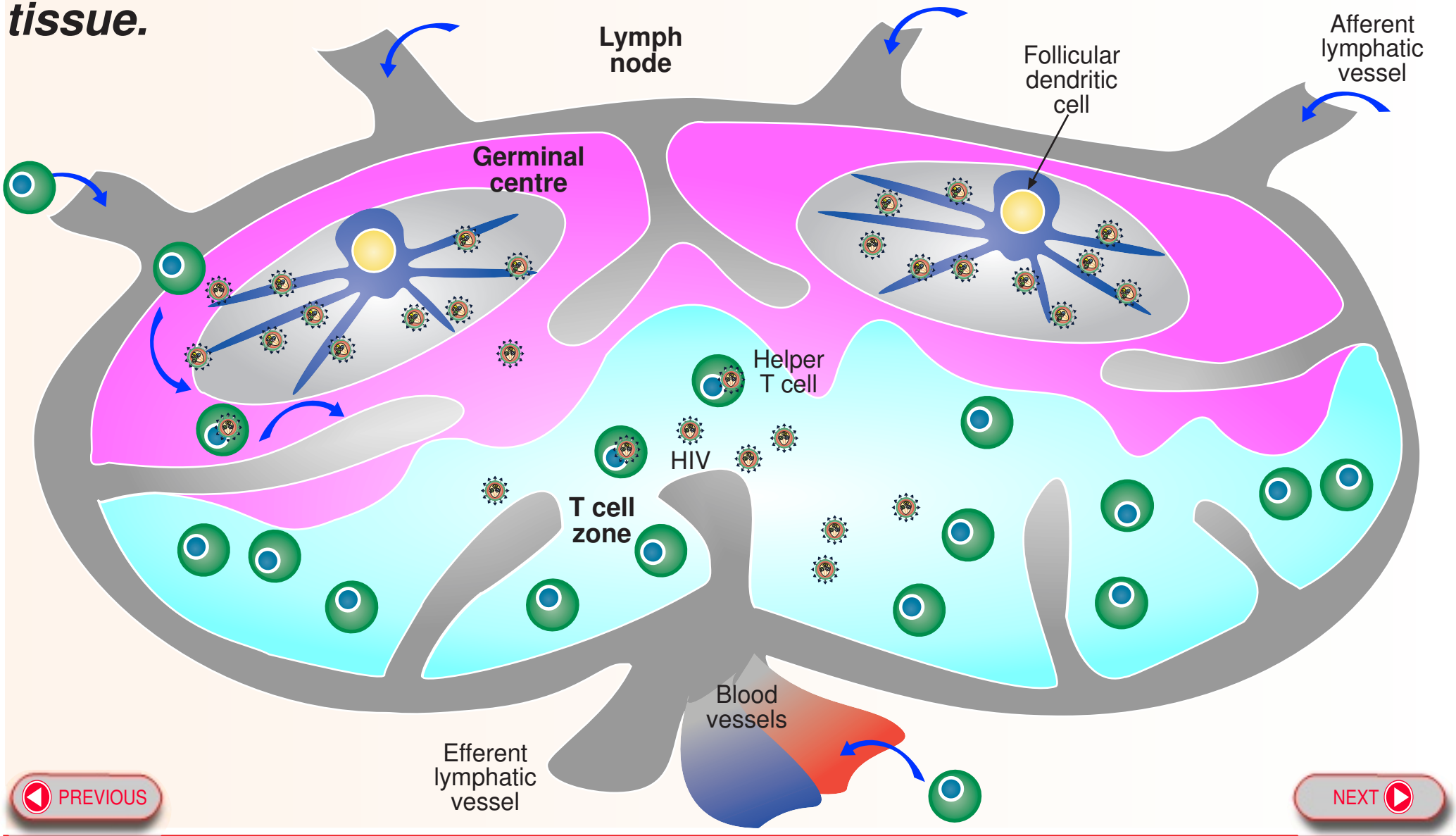
Preferential differentiation of pro-inflammatory CD4+ T cell phenotypes.



NEXT

Naive CD4+ T cells (Th0) interact with dendritic cells in the T cell zone of secondary lymphoid organs. Depending on the type of cytokine stimulation by dendritic cells, Th0 T cells can differentiate into Th1, Th2, Th17 or Treg phenotypes. Th1 and Th17 T cells secrete INF-γ and IL-17, respectively, which promote pro-inflammatory immune responses. Conversely, Th2 and Treg T cells secrete IL-10/IL-4 and IL-10, respectively, which antagonise pro-inflammatory immune responses by suppressing Th1 and Th17 T cell development. It is thought that IRIS may be due to an imbalance of pro-inflammatory and anti-inflammatory immune responses during the immune reconstitution phase that occurs shortly after initiation of ARV therapy.

HIV induced CD4+ T cell sequestration in secondary lymphoid tissue.

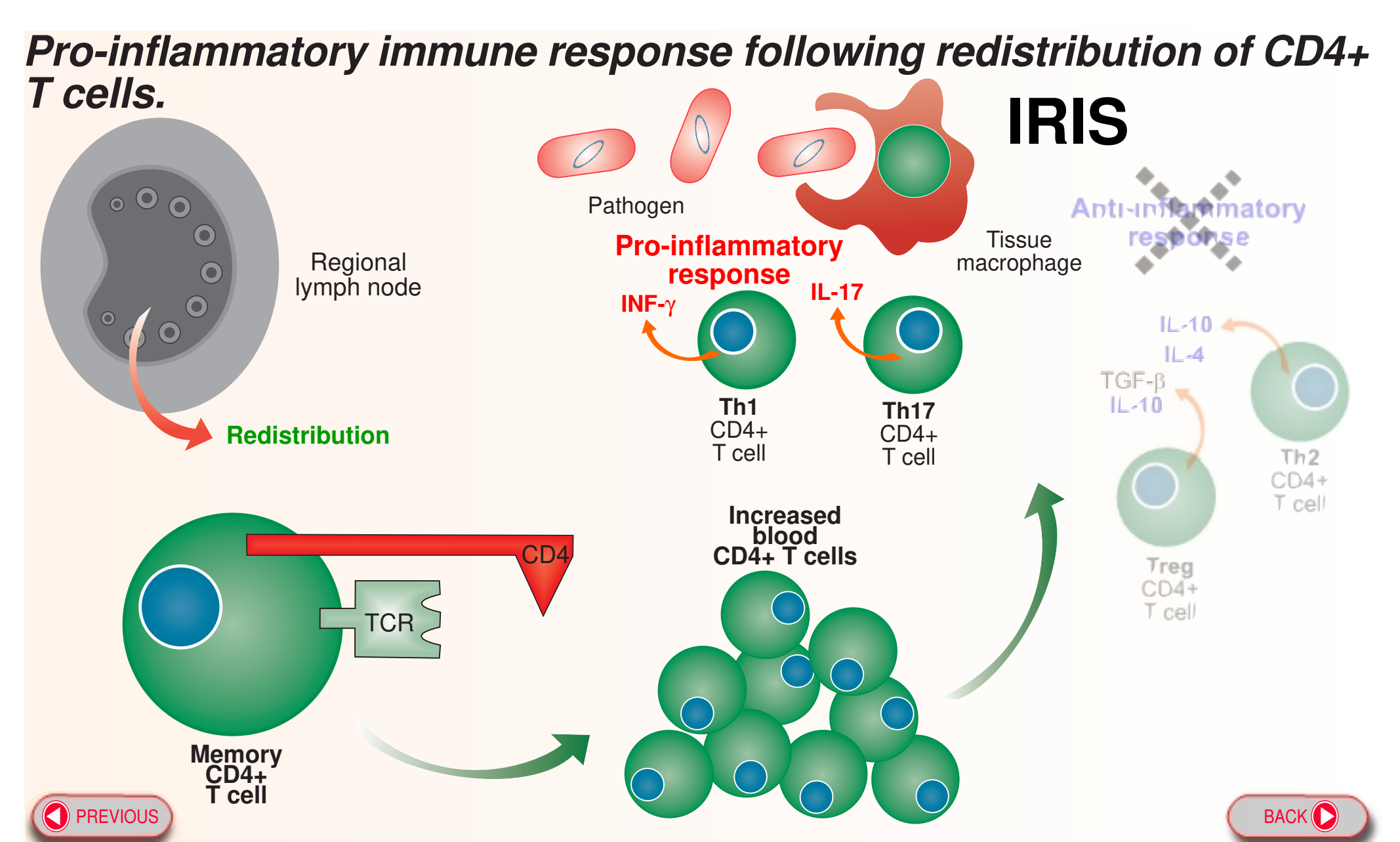


PREVIOUS

NEXT

Preferential replication of HIV in secondary lymphoid tissue results in accumulation of viral gp120, which interacts with CD4 receptors expressed on CD4+ T cells. CD4 receptor stimulation promotes retention of CD4+ T cells in the lymph node by interfererence with lymph node homing and exit receptor regulation. ARV therapy inhibits viral replication and reverses the sequestration of CD4+ T cells. The first phase of immune reconstitution following ARV therapy is the redistribution of sequestered CD4+ T cells from the lymph nodes to peripheral blood and tissues. It has been shown that the majority of these cells are of a memory phenotype that may initiate uncontrolled pro-inflammatory immune responses to recall antigens.

Pro-inflammatory immune response following redistribution of CD4+ T cells.



PREVIOUS

BACK

Soon after initiation of ARV therapy, a large reduction in levels in virus replication in lymphoid tissue leads to a reversal of CD4+ T cell sequestration in lymph nodes resulting in their redistribution to peripheral blood and tissues. The majority of these cells are of a memory phenotype that may initiate pro-inflammatory immune responses to recall antigens. In IRIS, it is thought that Th1 and Th17 T cells responding to recall antigens derived from living/dead organisms or antigens in tissue may result in uncontrolled inflammation due to an unbalanced anti-inflammatory response by Treg and Th2 T cells.