Negative immune regulators of T cells as targets for immunotherapy

Exacerbated immune activation is hallmark of HIV-1 infection leading to exhausted immune responses. Key mechanisms underlying this immune dysfunction involve the up-regulation and accumulation of multiple negative immune regulators on Ag-specific T cells such as PD-1, CTLA-4, CD160, Tim-3 and LAG-3. Triggering of these negative regulators with cognate ligands leads to a progressive, but reversible, loss of T cell functions. In this talk, I will present our results on the potential use of these negative regulators as targets for immunotherapy to reverse immune exhaustion and potentiate T cell responses in HIV-1 infection. These results include the combined blockade of PD-1 and CD160 negative pathways in primary T cells from HIV subjects ex vivo as well as the use of inhibitors of the immunosuppressive enzyme IDO in SIV-infected macaques as an experimental model for HIV infection. I will also present data on the role of certain negative immune regulators, herein CTLA-4, in the establishment of HIV-1 reservoirs. Our studies suggest that mechanisms leading to immune exhaustion of T cells are also involved in the long-term persistency of HIV-1 in the memory subset of CD4+ T cells.

Le vendredi 26 avril 2013 à 11 h 30
Pavillon Claire McNicoll, salle Z-260