LABEX IGO – 2023 INTERNAL CALL FOR PROJECTS FOR YOUNG INVESTIGATORS

Project title:
Enhancing the recognition of early HIV-infected cells by CD8+ T cells through modulation of the MHC class-I signaling axis

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Abstract:
Despite great advances in the treatment of HIV patients with combination antiretroviral therapies, there is still no available cures or vaccines. Treatments do not allow full clearing of the virus, notably due to viral reservoirs in resting CD4+ T cells committing HIV patients to life-long therapy. However rare patients called “HIV Controllers” or “non-progressors” are able to control the viremia without any treatment representing a nice model for a functional cure. Their immune system is known to be highly efficient, notably their HIV-specific CD8+ T response. I recently demonstrated the potency of CD8+ T cells from HIV controllers but not from progressors to recognize and kill HIV-infected CD4+ T cells right after viral entry into the cells before integration, *de novo* production or the establishment of latency. Such a recognition is induced by the presentation of peptides derived from incoming particles through the Major Histocompatibility Complex of class I (MHC-I) molecules.
In this project we propose to study the surface expression of the MHC-I molecules under early HIV-infection in activated and resting CD4+ T cells. We will then decipher whether its upregulation by key modulators will increase the CD8+ T cell response to early HIV-infected CD4+ T cells using a lymphoblastic cell line engineered to overexpress MHC-I and co-cultured with HIV-specific CD8+ T cell clones. Then, a collaboration with the Department of infectious diseases of Nantes University Hospital, will allow us to assess whether increased MHC-I/peptides surface expression on early HIV-infected CD4+ T cells is able to drive an efficient CD8+ T cell response in a fully autologous co-culture system with cells from HIV-infected individuals.