## Cellular and tissue reservoirs of HIV/SIV

### PE10 Progressive contraction of the latent HIV reservoir around a core of less-differentiated CD4+ memory T-cells

Jaafoura S.[1], De Goer De Herve M.G.[1], Hernandez-Vargas E.A.[2], Hendel-Chavez H.[1], Abdoh M.[1], Mateo M.C.[1], Krzysiek R.[3,4], Merad M.[5], Seng R.[6], Tardieu M.[1,4], Delfraissy J.F.[1,4,7], Goujard C.[4,5,7], Taoufik Y.[1,4]
*[1]INSERM U 1012, Le Kremlin Bicetre, France, [2]Helmholtz Centre for Infection Research, Braunschweig, Germany, [3]INSERM U 996, Clamart, France, [4]Faculté de Médecine, Université Paris-Sud, Le Kremlin Bicetre, France, [5]Institut Gustave Roussy, Department of Medicine, Villejuif, France, [6]INSERM U 1018, Le Kremlin Bicetre, France, [7]Hopitaux Universitaires Paris-Sud, Department of Internal Medicine, Le Kremlin Bicetre, France*

**Background:** HIV can persist within a small pool of long-lived resting memory CD4+ T cells infected with integrated latent virus. This latent reservoir involves several memory CD4+ T-cell subsets at distinct differentiation stages with different phenotypic and functional properties, forming distinct sub-reservoirs. Precise immunological characterization of the latent reservoir, including the size of each sub-reservoir, is important for the complex challenge of 'therapeutic purging'. The relative size of each sub-reservoir may depend on its decay rate and may therefore vary according to the time on ART. Here, we determined the decay rates of latently infected resting memory subsets.

**Methods:** We conducted a cross-sectional study on 45 strictly selected homogeneous patients. Inclusion criteria were: plasma virus load undetectable for 24 to 189 months without any viral blip and a CD4 T cell count higher than 500/ mm3 of blood. Highly purified memory CD4 T-cell subsets were sorted: stem cell memory CD4 T cells (TSCM), central memory CD4 T cells (TCM), effector memory CD4 T cells (TEM), and an additional subset with an intermediate phenotype (TIM). Integrated HIV DNA was quantified in these cells by ALU-gag PCR. To take into account inter-patient variability, we performed a mathematical modeling (Monte Carlo algorithm).

**Results:** Our results suggest a progressive reduction of the size of the blood latent reservoir around a core of less-differentiated memory subsets (central memory (TCM) and stem cell-like memory (TSCM) CD4+ T cells). This process appears to be driven by the differences in initial sizes and decay rates between latently infected memory subsets. Our results also suggest an extreme stability of the TSCM sub-reservoir, the size of which is directly related to cumulative plasma virus exposure before the onset of ART.

**Conclusions:** Latently infected TCM and TSCM should be a priority target for therapeutic strategies. Our results stress the importance of early initiation of effective ART to limit the size of the TSCM sub-reservoir.