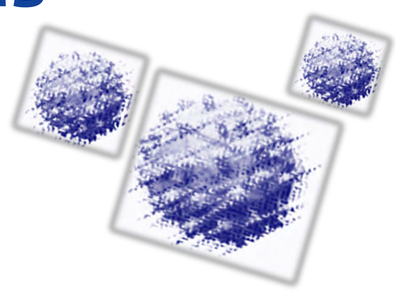
00318

Characterization of CD8⁺ Resident Memory T cells towards the control of the HIV reservoir in the Cervical Mucosa



Núria Massana[1], Jon Cantero-Pérez[1], Judith Grau-Expósito[1], Laura Luque-Ballesteros[1], Josep Castellví[2], Laura Mañalich-Barrachina[3], Cristina Centeno-Mediavilla[3], Vicenç Falcó[1], María J. Buzón[1], Meritxell Genescà[1]*

[1]Department of Infectious Diseases, Hospital Universitari Vall d'Hebrón, Institut de Recerca (VHIR), Universitat Autònoma de Barcelona, Barcelona, Spain; [2]Department of Pathology, Hospital Universitari Vall d'Hebrón, Universitat Autònoma de Barcelona, Barcelona, Spain; [3]Department of Obstetrics and Gynecology, Hospital Universitari Vall d'Hebrón, Universitat Autònoma de Barcelona, Barcelona, Spain.

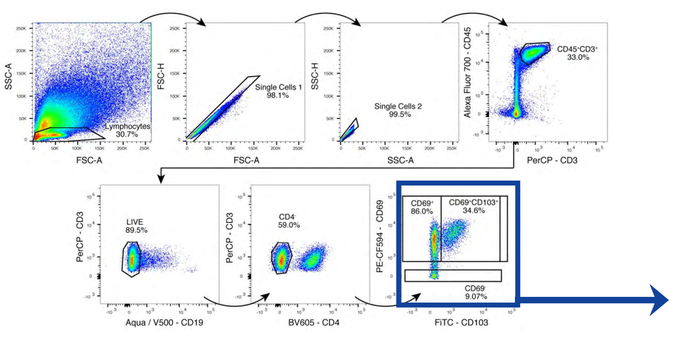
BACKGROUND

In tissues, resident memory CD8⁺ T cells (T_{RM}) are most likely necessary to eliminate remaining cellular HIV-1 reservoirs. However, T_{RM} signature includes expression of molecules associated to exhausted phenotypes during chronic viral infections. Here we addressed the functional capacity of CD8⁺ T_{RM} from the cervical mucosa of HIV-infected women on ART to determine the most effective phenotypes at limiting viral persistence.

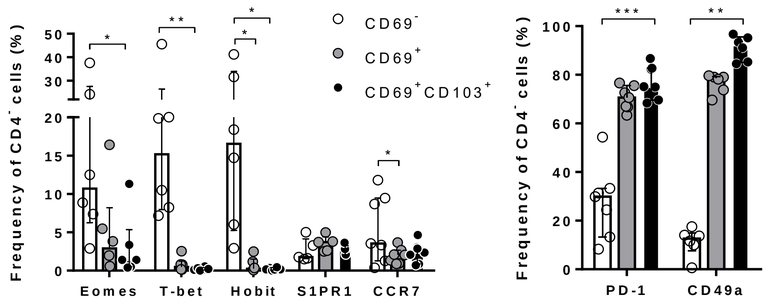
METHODS and RESULTS

CD8⁺ T cells from cervical tissues were phenotyped based on CD69 expression to determine T_{RM} signature (n=6-9). Frequency and activation of CD103⁺/⁻ CD8⁺ T_{RM} subsets were compared between healthy (n=9) and ART-suppressed HIV⁺ women (n=18). In a subset of these patients, we determined total vDNA in blood and cervix (n=7). A functional assay was established to determine suppression of viral reactivation by CD8⁺ T_{RM} in ART-suppressed HIV⁺ women.

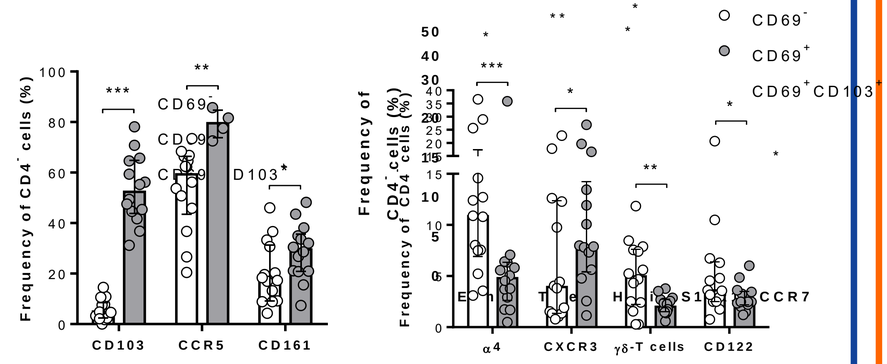
Gating Strategy



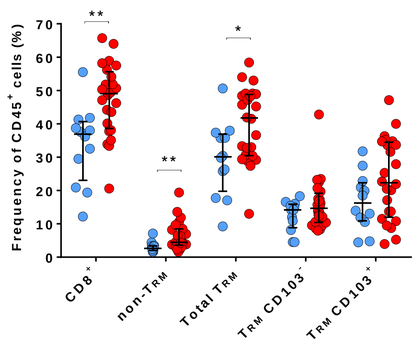
Cervical CD69⁺ CD8⁺ are bona fide T_{RM}



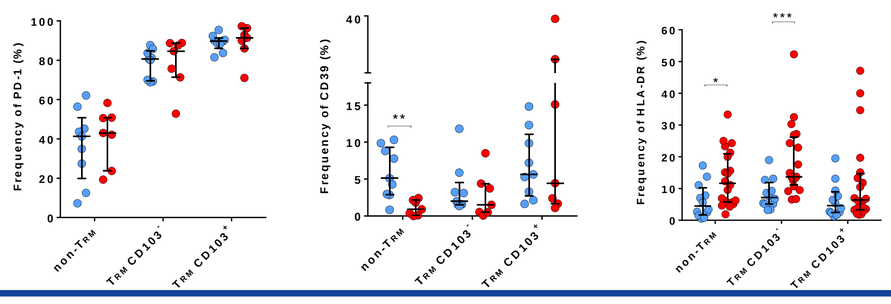
CD8⁺ T_{RM} express more CXCR3, CCR5, CCR2 and CD161 and less α4, CD122 and γδTCR compared to non-CD8⁺ T_{RM}



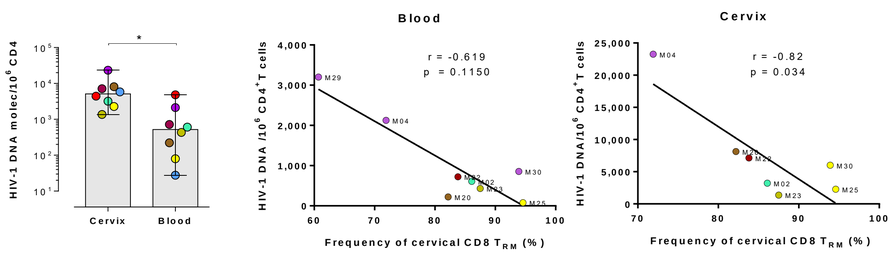
Impact of HIV on cervical CD8⁺ T cells from ART-treated HIV patients



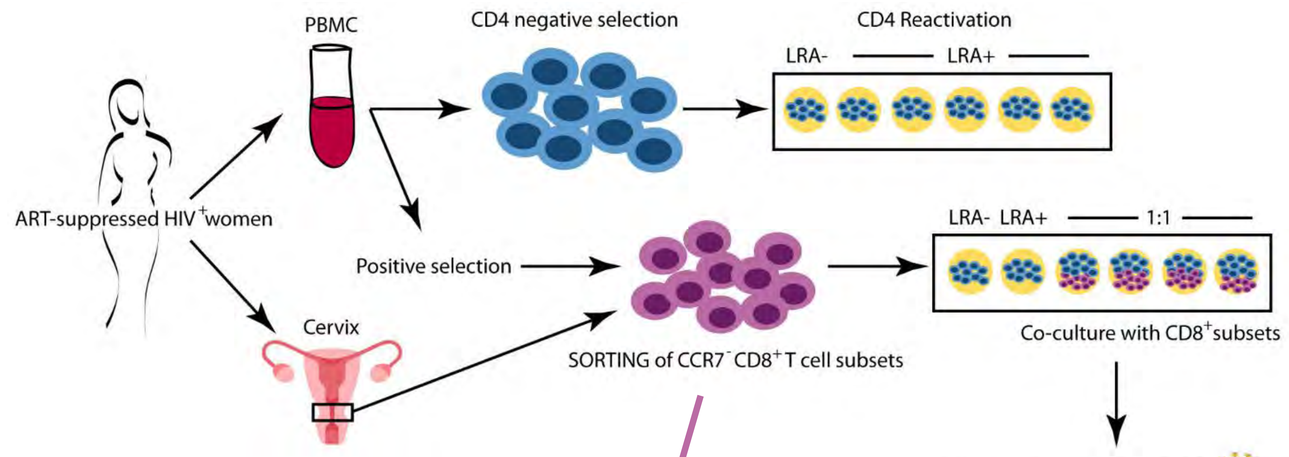
Higher frequencies of CD8⁺ T_{RM} and non-T_{RM} expressing more HLA-DR



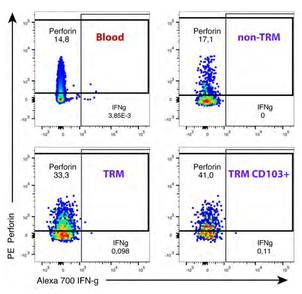
Frequency of CD8⁺ T_{RM} correlates with proviral DNA

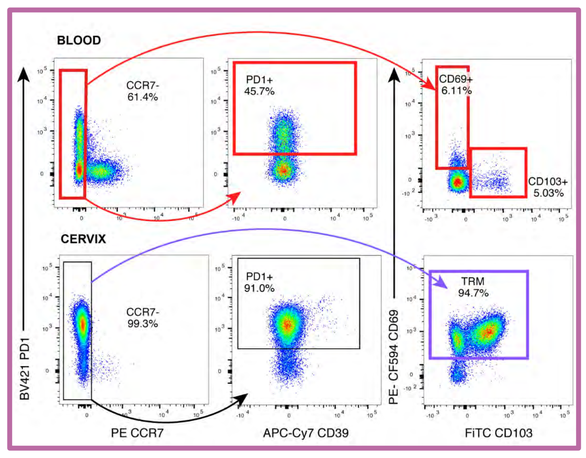


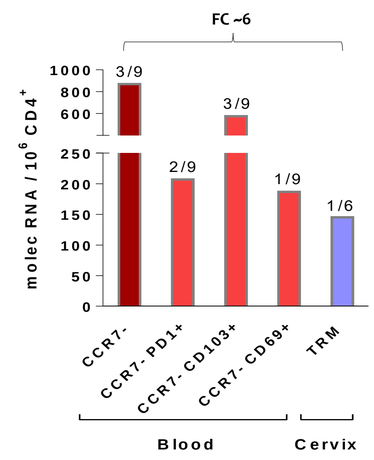
CD8⁺ T_{RM} from ART-treated HIV patients control de viral reservoir



Higher baseline expression of perforin in cervical CD8⁺ T_{RM}

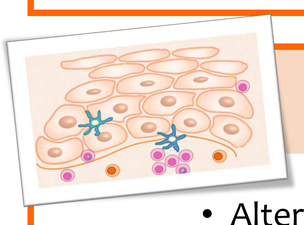






Frequency of CD8⁺ T_{RM} correlates with proviral DNA

DISCUSSION and CONCLUSIONS



- Alterations of the CD8⁺T cell compartment within the cervical mucosa remain in HIV⁺ women even after several years of effective ART-suppression.
- The association between higher proportion of CD8⁺T_{RM} in cervix and less proviral HIV-1 DNA, together with data showing higher control of virally-reactivated infected cells by CD8⁺T_{RM}, indicates that these cells may be critical to control persisting virus in tissues.

ACKNOWLEDGMENTS. This work was supported by the PI17/01470 project, integrated in the National R + D + I and funded by the ISCIII-General Evaluation Branch and the European Regional Development Fund (FEDER) and a fellowship from Dexeus foundation. MG is currently supported by a contract to scientist funded by the *Pla estratègic de recerca i innovació en salut* (PERIS, SLT002/16/00353), JC by a fellowship from Gilead Sciences (GLD18-00008) and NM by a Project funded by *La Fundació la Marató de TV3* (20181410).

***meritxell.genesca@vhir.org**