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Chemokine receptors expression analysis reveals heterogeneity among central memory CD8 T cells, identifying different migratory patterns between HIV-infected patients

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Abstract

Statement of the Problem: Among HIV-infected patients, a rare proportion of patients (<0.5%) are able to spontaneously control the virus, in the absence of antiretroviral treatment (ART). Numerous studies aim to decipher the crucial difference in the immune responses developing in these HIV-controllers (HIC) patients. Memory differentiation, cytotoxic function, exhaustion and senescence profile of the T cell compartment in the various groups of patients have been evaluated. Recent publications demonstrate the importance of the migratory phenotype to identify crucial CD8 T cell responses in the context of chronic infection. The objective of the study was to readdress the functional activity of CD8 T cell in HIV infection by evaluating the chemokine receptor expression. The aim was to determine whether HIC patients might differ from ART-treated patients when considering CD8 T cell migratory properties. Methodology & Theoretical Orientation: 37 HIV-infected patients including HIC or ART patients and 15 healthy subjects were studied. The expression of CXCR3, CXCR5 and CX3CR1 was evaluated in combination with standard markers of T cell memory differentiation (CCR7 (and CD62L), CD45RO, CD27, CD28) and exhaustion (PD-1, TIGIT). Flow cytometry was performed on fresh whole blood samples. Findings: When performing tSNE analyses, we observed that the central memory (Tcm) CD8 T cell compartment included highly heterogeneous clusters. The analyses of diverse chemokine receptors confirmed this heterogeneity in particular among CXCR3, CXCR5 or CXCR3/CXCR5 coexpressing cells. HIV infected patients, both HIC and ART, exhibited a higher fraction of CXCR3+/CXCR5+ cells among Tcm than HD. Interestingly, HIC patients exhibited lower proportion of CXCR3+/CXCR5- among Tcm than ART patients. Conclusion & Significance: The difference in the expression of chemokine receptors on Tcm CD8 T cells in HIC versus ART patients may reflect different homing properties and may directly impact the quality of CD8 T cell responses.

Biography:

Dr Christine Bourgeois has her expertise in the characterization of T cell immune responses. Her research activities currently focus on the regulation processes affecting T cell responses notably in the context of chronic infections (including Treg mediated suppression, exhaustion, senescence). These studies are developed both in clinical context (ageing, HIV infection) but also in various experimental animal models (mice, non-human primates, humanized mice, humans). The current focus of her group is the evaluation of local and systemic pathways regulating immune T cell responses. Because chronic infection may highly rely on the immune responses developing specifically in lymphoid but also at reservoir site, our work includes studies on the migratory profile of CD8 T cells in the blood and studies of the immune potential of adipose tissue that has been identified as a reservoir site for HIV infection. Obesity/diabetes and cardiovascular dysfunction. A component of these endeavors is distinguishing contributions of oxidants from uric acid in driving the inflammatory phenotype.

Publications

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3. Laparra A et al (2019) The Frequencies of Immunosuppressive Cells in Adipose Tissue Differ in Human, Non-human Primate, and Mouse Models. Front Immunol. 10:117.

4. Damouche A et al (2017) High proportion of PD-1-expressing CD4+ T cells in adipose tissue constitutes an immunomodulatory microenvironment that may support HIV persistence. Eur J Immunol. 47(12):2113-2123

5. Damouche A et al (2015) Adipose Tissue Is a Neglected Viral Reservoir and an Inflammatory Site during Chronic HIV and SIV Infection. PLoS Pathog.11(9):e1005153.

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