

CONFERENCE

CAHR
2022

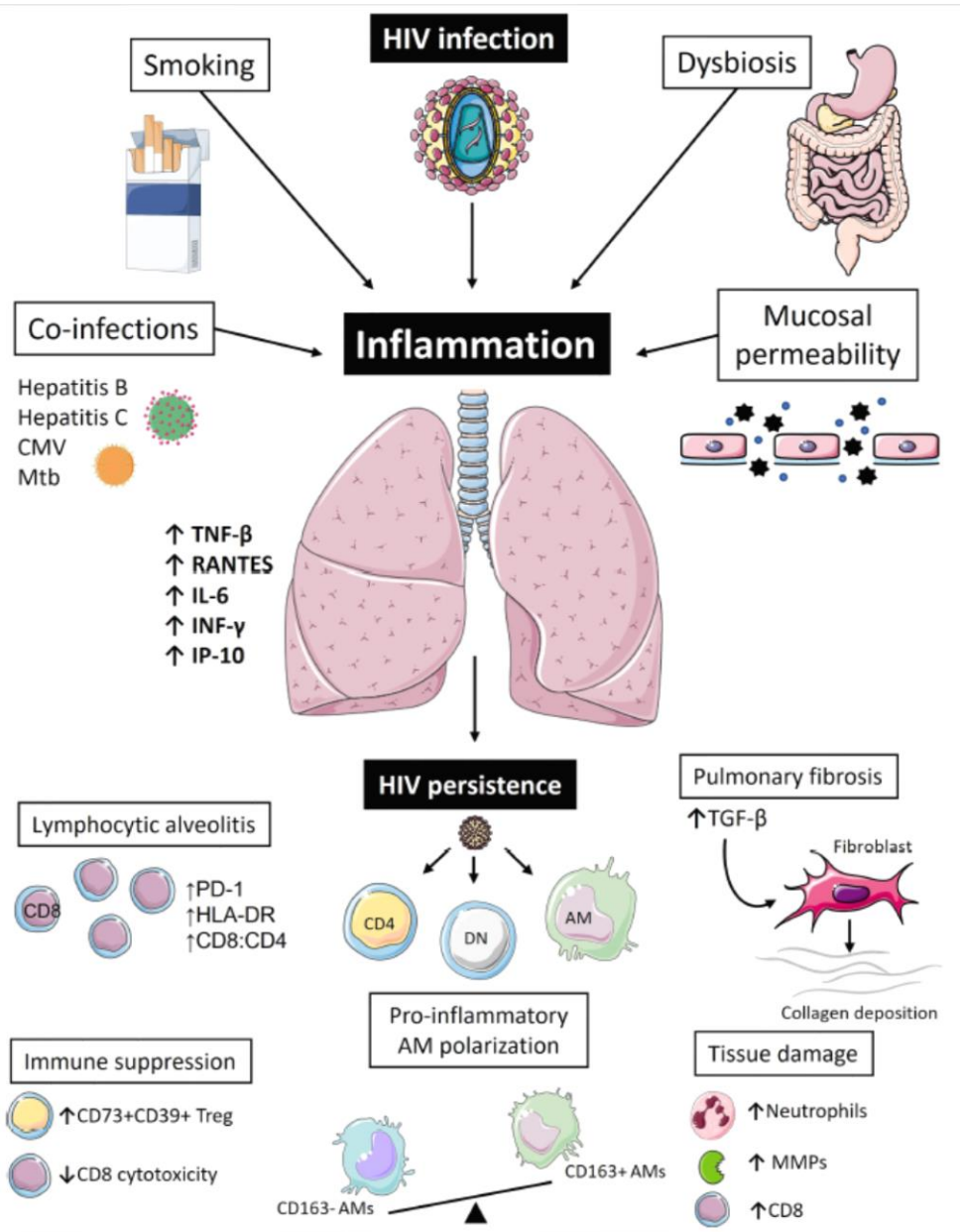
VIRTUAL

April 27 to 29, 2022

Effects of HIV-infection and Smoking on Pulmonary Mucosal Tissue-resident CD8 T-Cell Dynamics in Era of Antiretroviral Therapy

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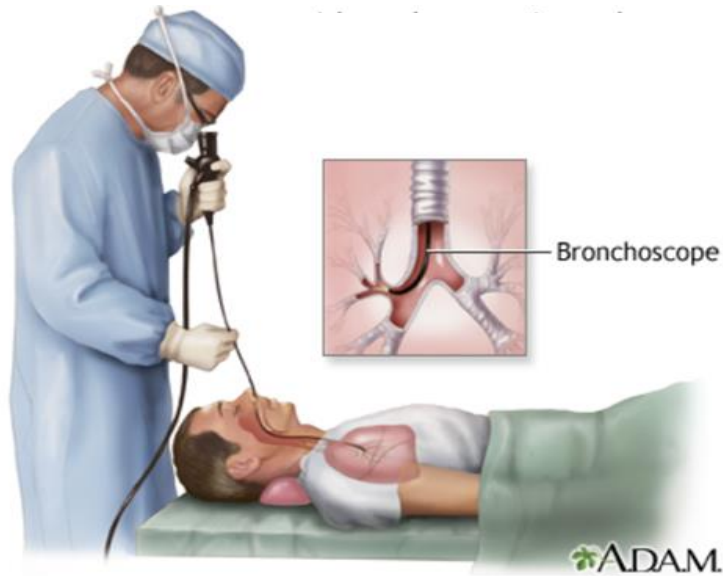
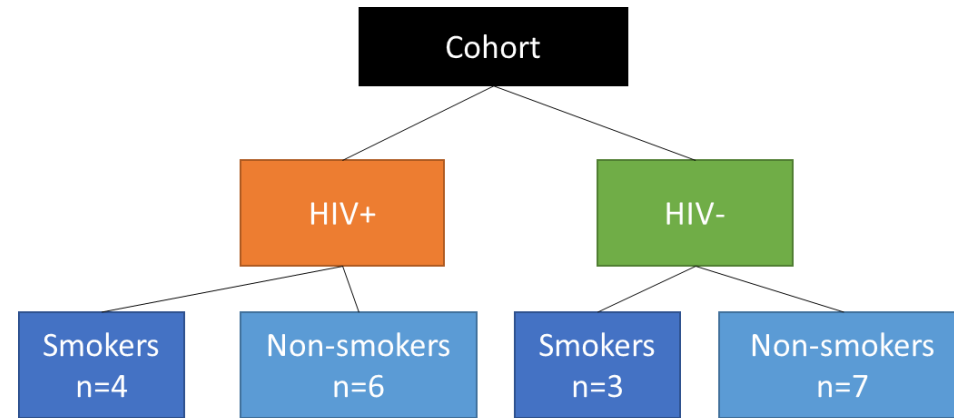


- HIV is associated with higher risk of lung disease**
 - Rates of primary lung cancer, bacterial pneumonia, influenza, COPD, and tuberculosis in ART-naïve HIV-infected patients are significantly higher than in uninfected individuals. (*Costiniuk, Jenabian, Rev Med Virol 2014*)
 - Lymphocytic alveolitis is common, characterized by infiltration of functionally impaired CD8 T-cells into the lung (*Neff et al., Am J Respir Crit Care Med. 2015*)
- Smoking leads to inflammation and immune dysregulation**
 - Cigarette smoke exposure can induce a significant increase in cytotoxic CD8 -cells in BAL (*Hodge et al., Clin Exp Immunol 2011*)
 - Smoking and HIV** are two **independent** risk factors for COPD development (*Lalloo et al., Respirology 2016*)
 - Pulmonary emphysema is more prevalent in HIV+ smokers compared to seronegative smokers and is often developed at a younger age (*Petrache et al., Thorax 2008*)
- CD8 T-cells are required for HIV control**
 - Once HIV-specific CD8 T-cells rise during acute infection, peak viremia begins to subside (*Collins DR. et al., Nat Rev, 2020*)
 - CD8 T-cell depletion in SIV-infected Rhesus Macaques treated with short-term ART, leads to increased plasma viremia, which is reversible with CD8 T-cell repopulation (*Cartwright, E. K., et al. 2016*)
- Lung CD8 Trm are indispensable for optimal protection against pulmonary virus infection**
 - CD8 Trm persist in the lung following resolution of a respiratory virus infection and provide first-line defense against reinfection (*Snyder et al., Curr Opin Immunol. 2019*)

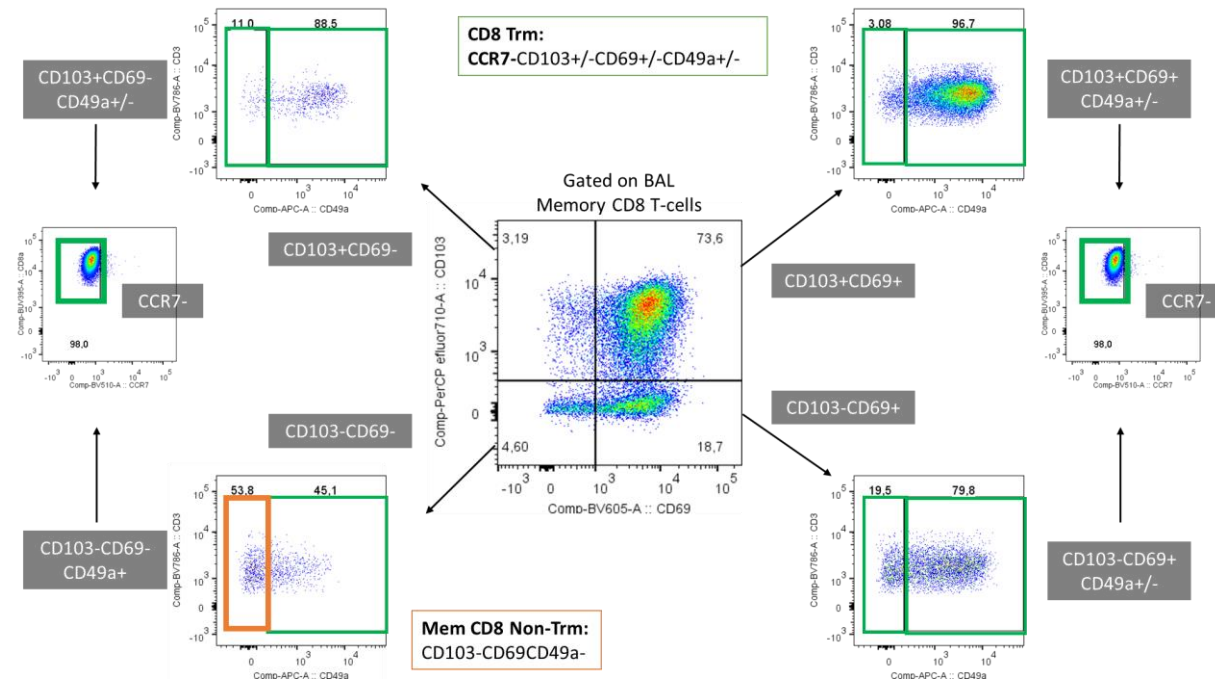
Four groups of participants will be recruited at the McGill University Health Centre:

- **ART treated PLWH** (suppressed VL ≥ 3 years) **smokers** and **non-smokers**
- **uninfected smokers** and **non-smokers**

50-100 ml of **BAL fluid** obtained via bronchoscopies and matched 40ml **blood** samples will be collected by venipuncture

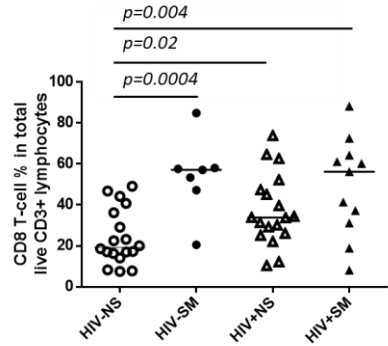


Gating strategy: Stratifying Trm subsets among live single cell memory CD8 T-cells from BAL fluid

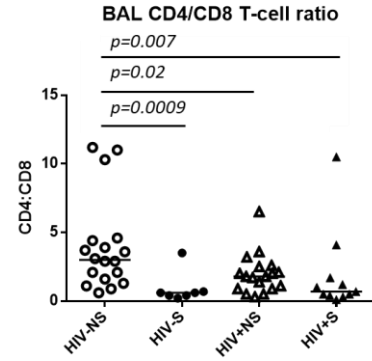


Smoking and positive HIV status **independently** associated with significantly **higher CD8 T-cell %** and **lower CD4:CD8 ratio**

A. BAL CD8 T-cell frequency

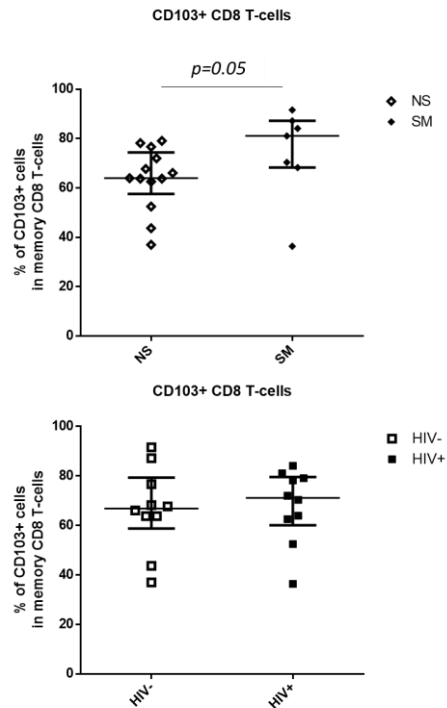


B. BAL CD4/CD8 T-cell ratio

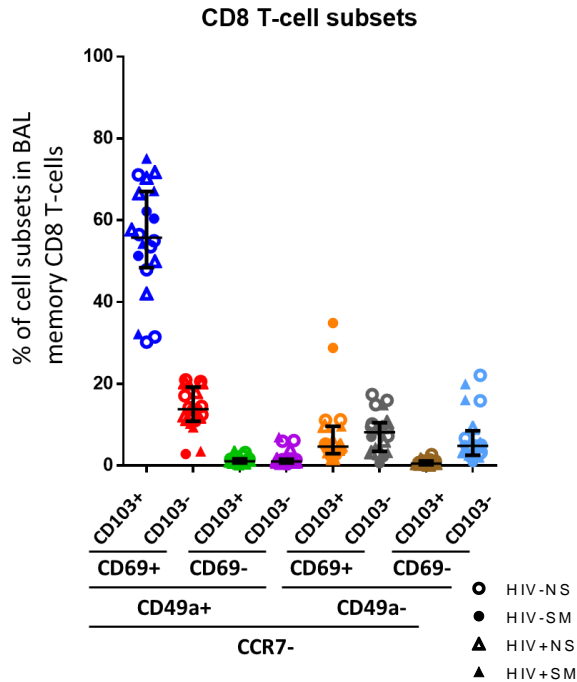


Smoking associated with higher % of CD103+ CD8 T-cells in BAL

C. CD103+ CD8 T-cells

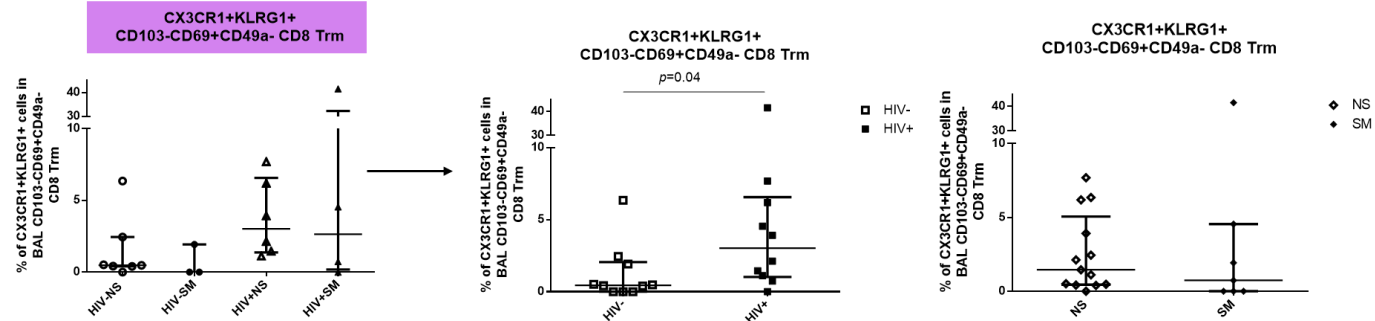


D. BAL CD8 T-cells: major Trm subsets



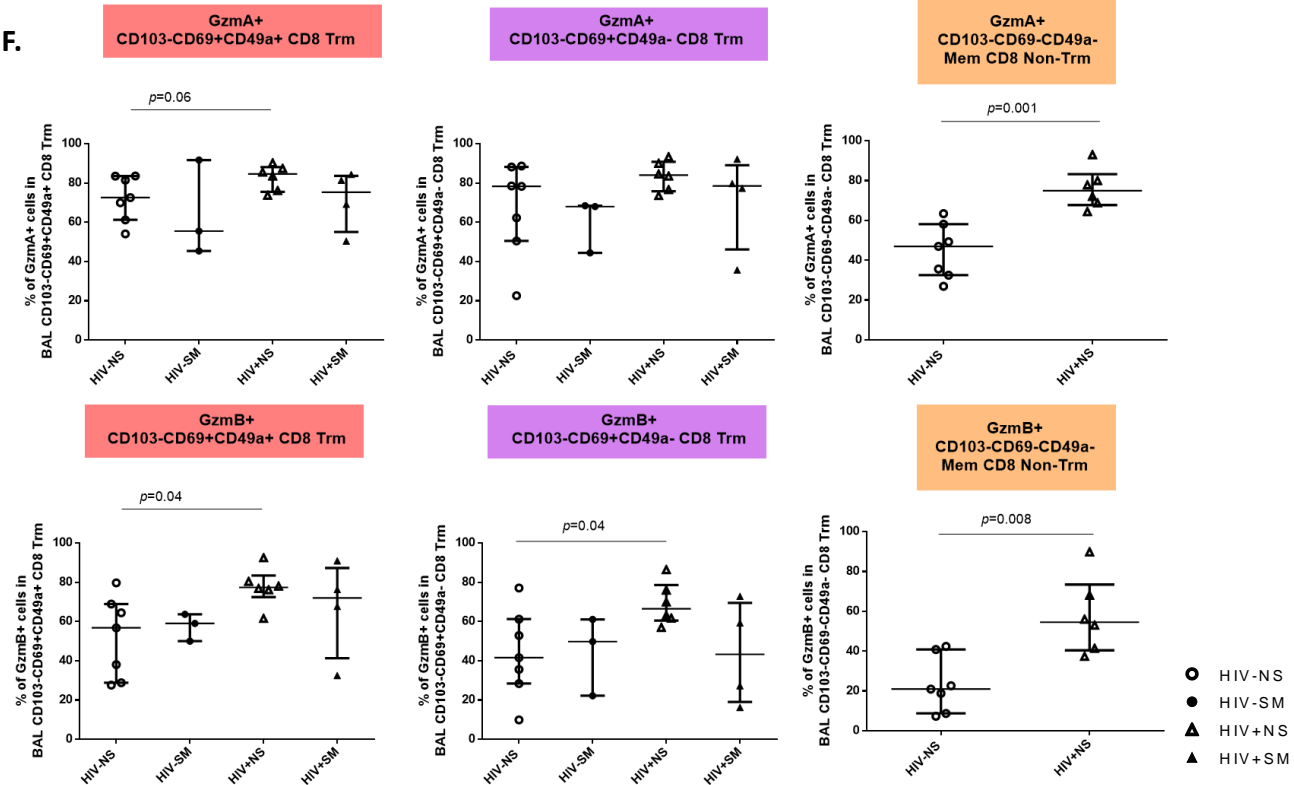
HIV+ status associated with higher % of CX3CR1+KLRG1+ CD8 T-cells

E.

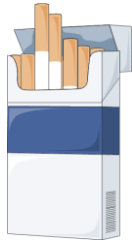


HIV+ status associated with higher levels of GzmA/B in CD103- CD8 T-cells

F.



HIV and smoking have distinct and different effects on lung mucosal CD8 T-cell dynamics

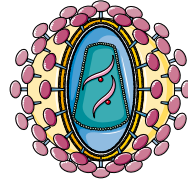


Smoking:

- ↑ CD8Trm retention via upregulation of CD103



CD8 Trm accumulation and retention



HIV:

- ↑ GzmA/B expression
- ↑ % of CD8 Tem from the periphery



GzmA/B+ CD8 T-cell accumulation



Contribute to:

Lymphocytic alveolitis
COPD
Emphysema

Acknowledgements

