



Impact of early antiretroviral therapy on tissue resident myeloid cells in the liver and lung of SIV-infected rhesus macaques

Poster : PP 2.1

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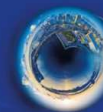
Research director : Dr Jérôme Estaquier





CONFLICTS OF INTEREST

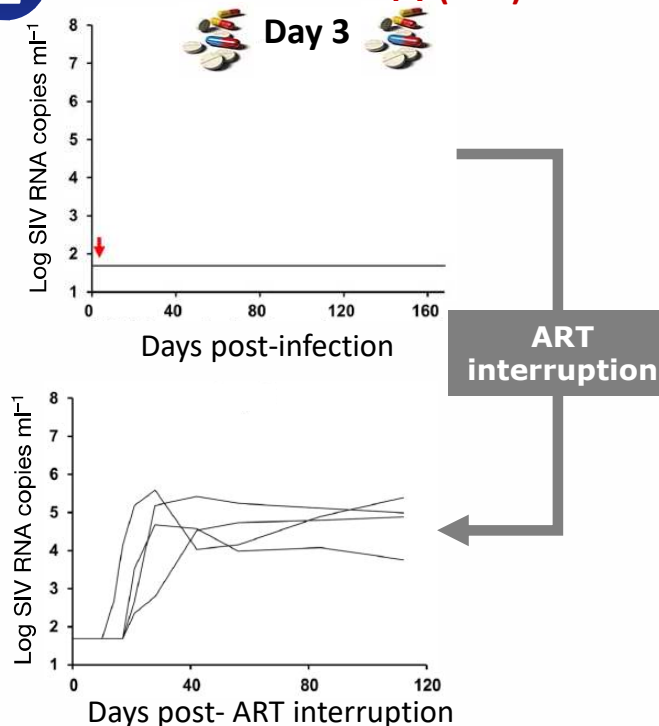
No conflict of interest to disclose



Scientific Background

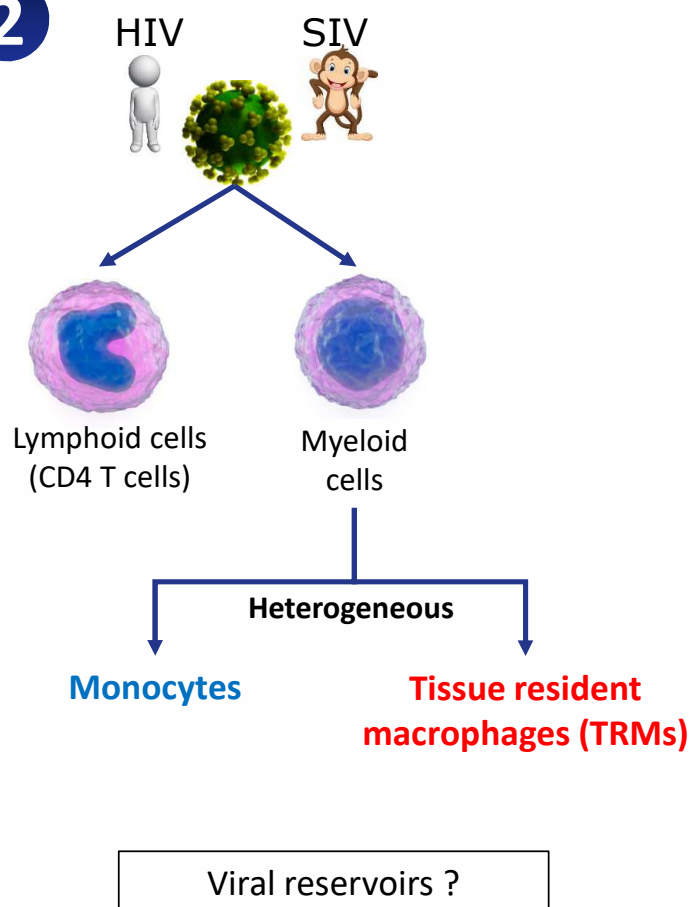
1

Antiretroviral therapy (ART)

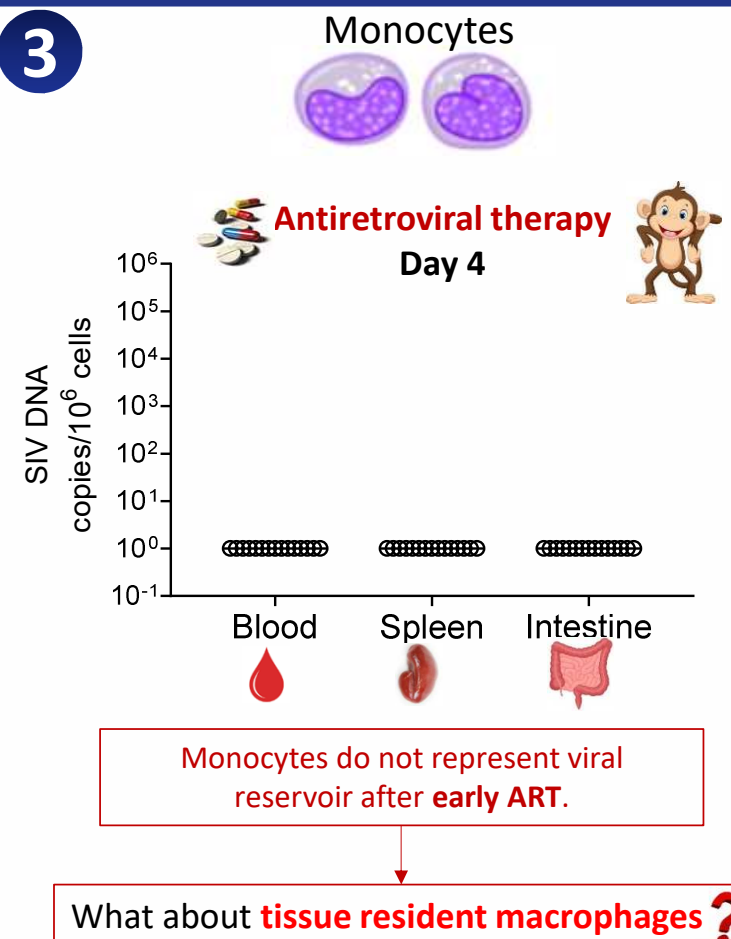


Viral rebound demonstrates early viral dissemination and viral reservoir establishment in deep tissues

2



3



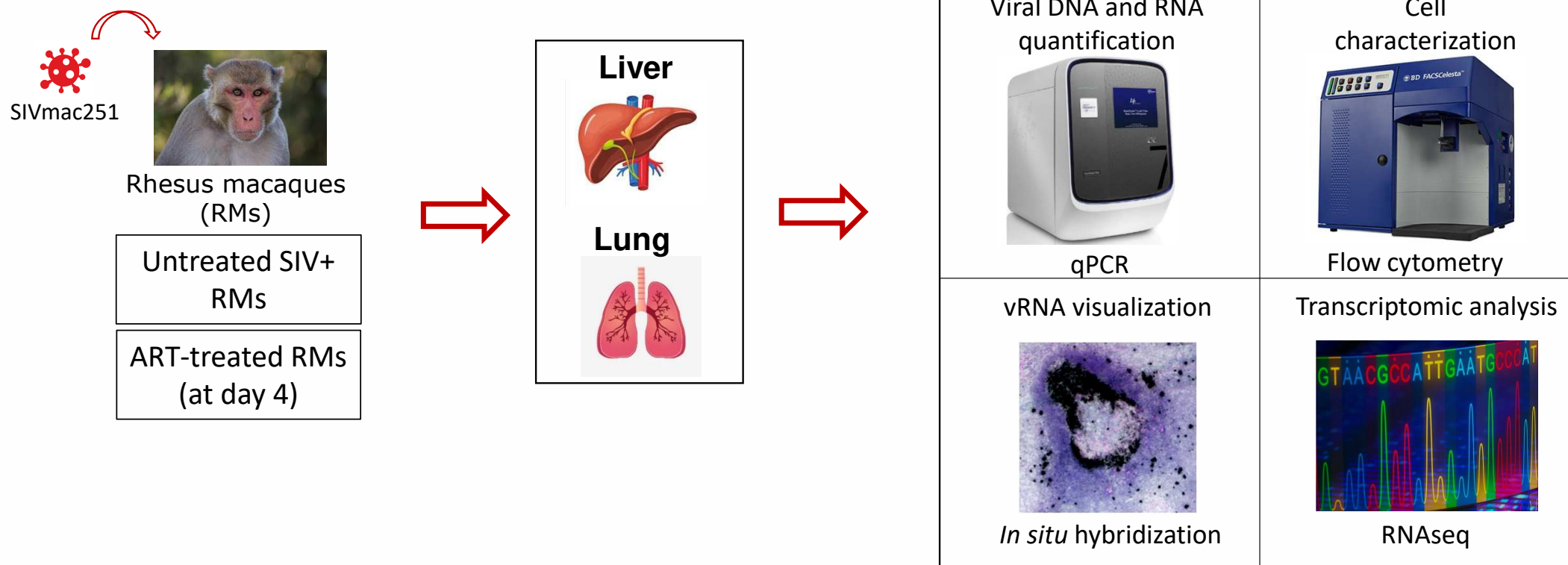
Clain J., Rabezanahary H. et al., 2020

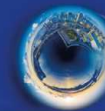
Whitney et al, Nature, 2014.



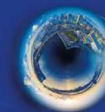
Objectives and experimental procedure

General objective : To assess the role of tissue resident macrophages (TRMs) in viral seeding in the liver and lung.

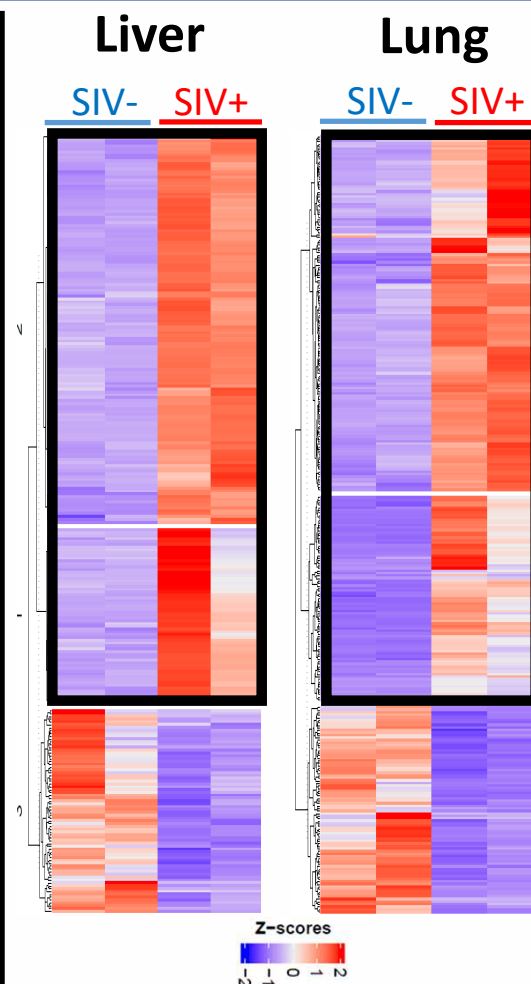
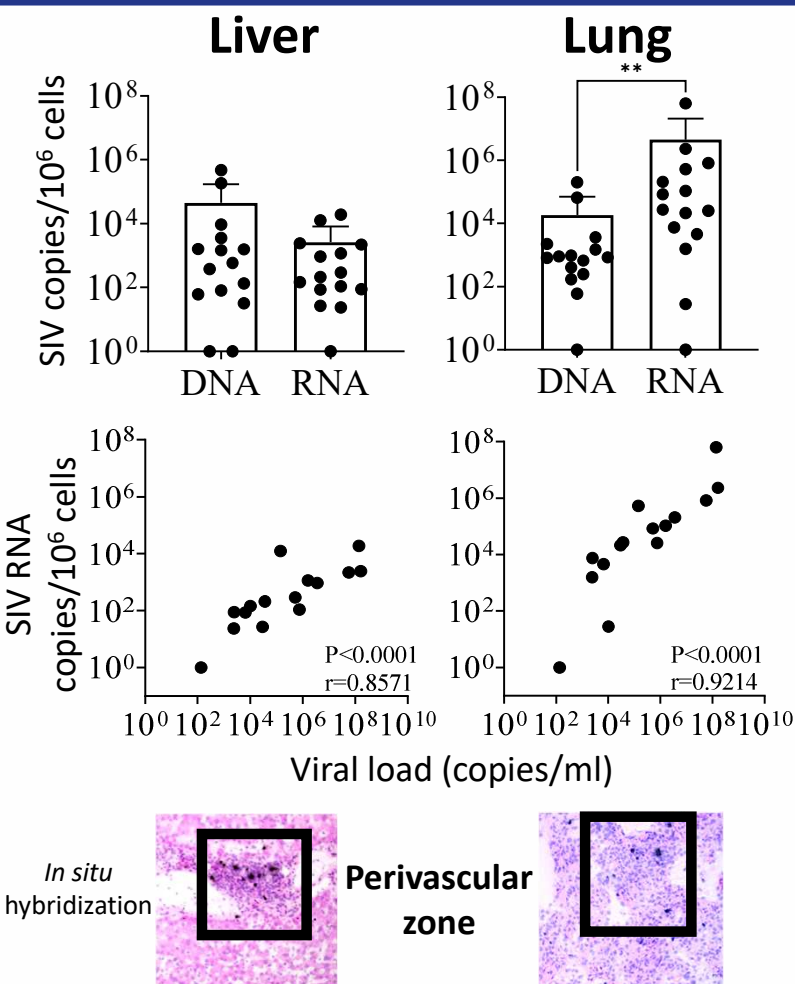




Objective 1 : Viral infection in the liver and lung of untreated monkeys



Results



Liver and lung of SIV-infected monkeys present an important innate immune profile

↗ **inflammatory response markers** : CXCL8/9/10/11, C1QB, C1QC, CCR1, CD300A, FPR1/3, S100A8/9, NCF1/2, CSF3R

↗ **myeloid cell markers** : STAT1, TLR4, CD86, CD32, CD68, CD163, CXCR2, MARCO

↗ **ISG markers** (interferon-stimulated genes) : ISG15/ISG20, IFIT, IRF, TRIM, DDX58/60, OAS

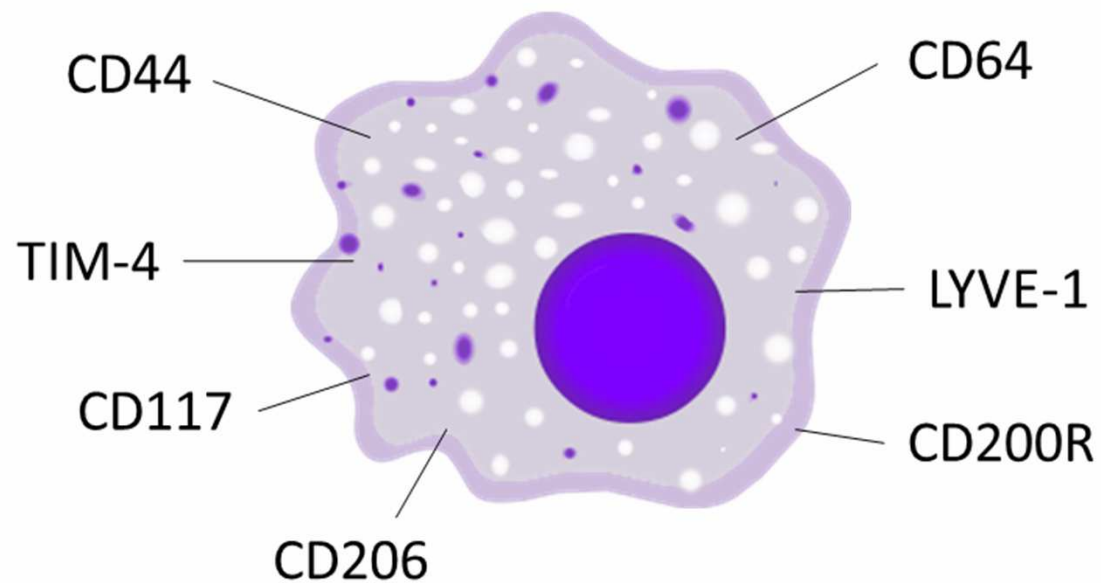


Objective 2 : Characterization of TRMs in the liver and lung



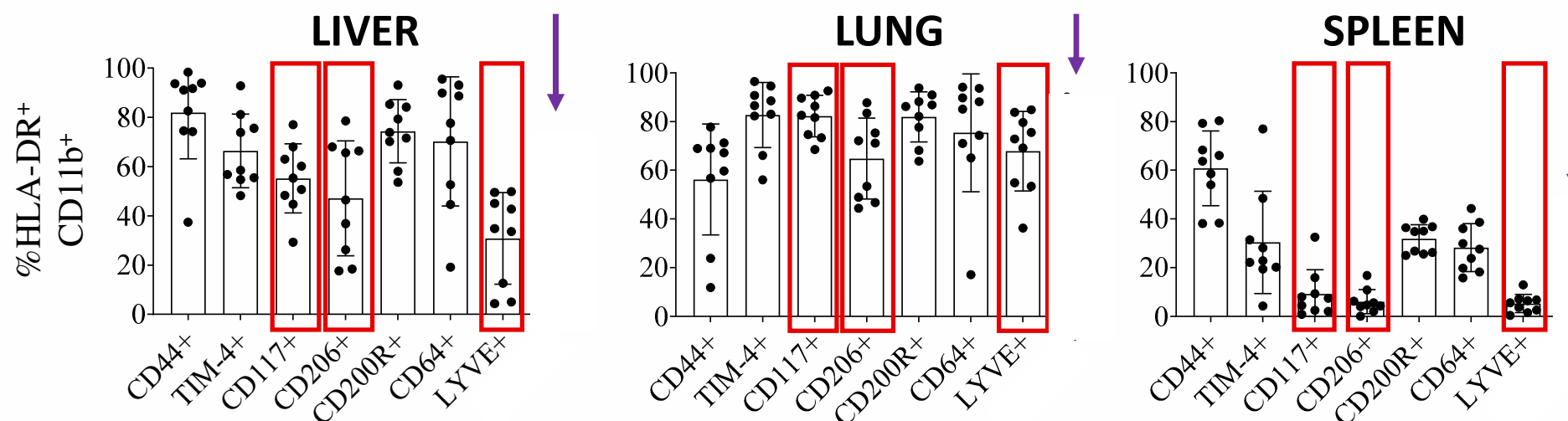
Results

**Tissue Resident Macrophage markers
mostly defined in newborn mice**





Results



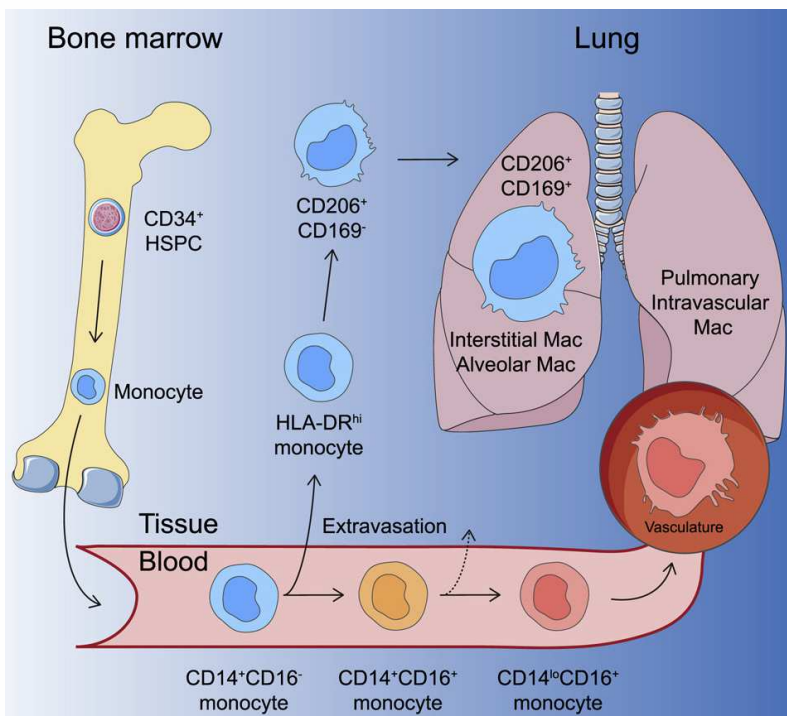
The phenotype of macrophages in infected monkeys indicated that CD117, CD206 and LYVE-1 could be markers of interest to specifically define tissue macrophages.

CXCR3 (CXCL10 receptor) :
Involved in cell recruitment to inflammation sites.

Tissue macrophages may be recruited in inflamed tissues

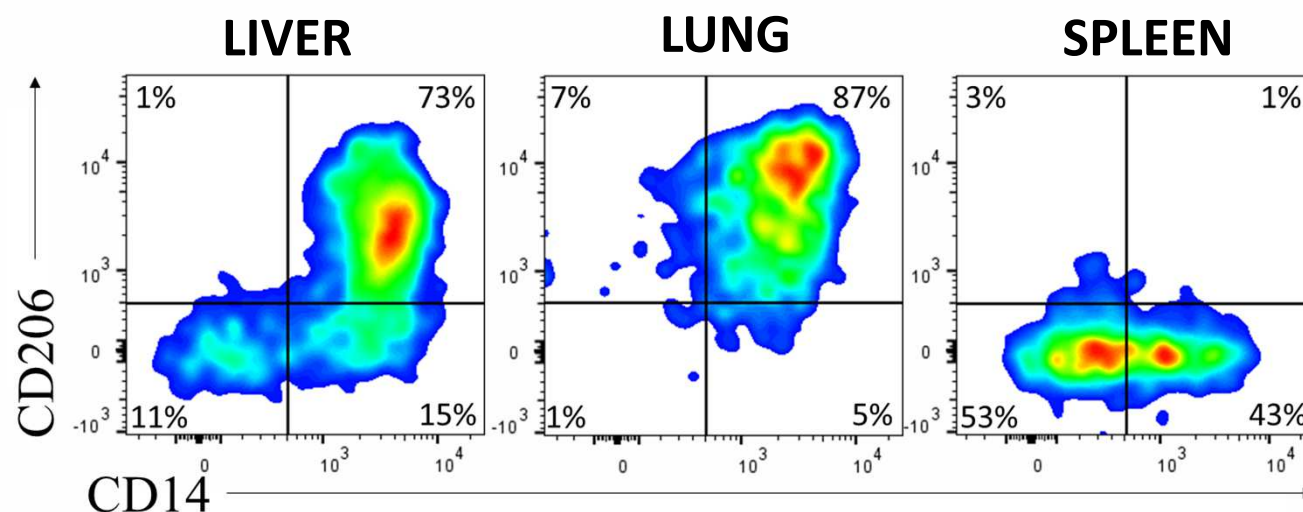


Results

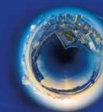


Evren E et al., Immunity 2021

Monocytes infiltrating the tissue may acquire CD206.



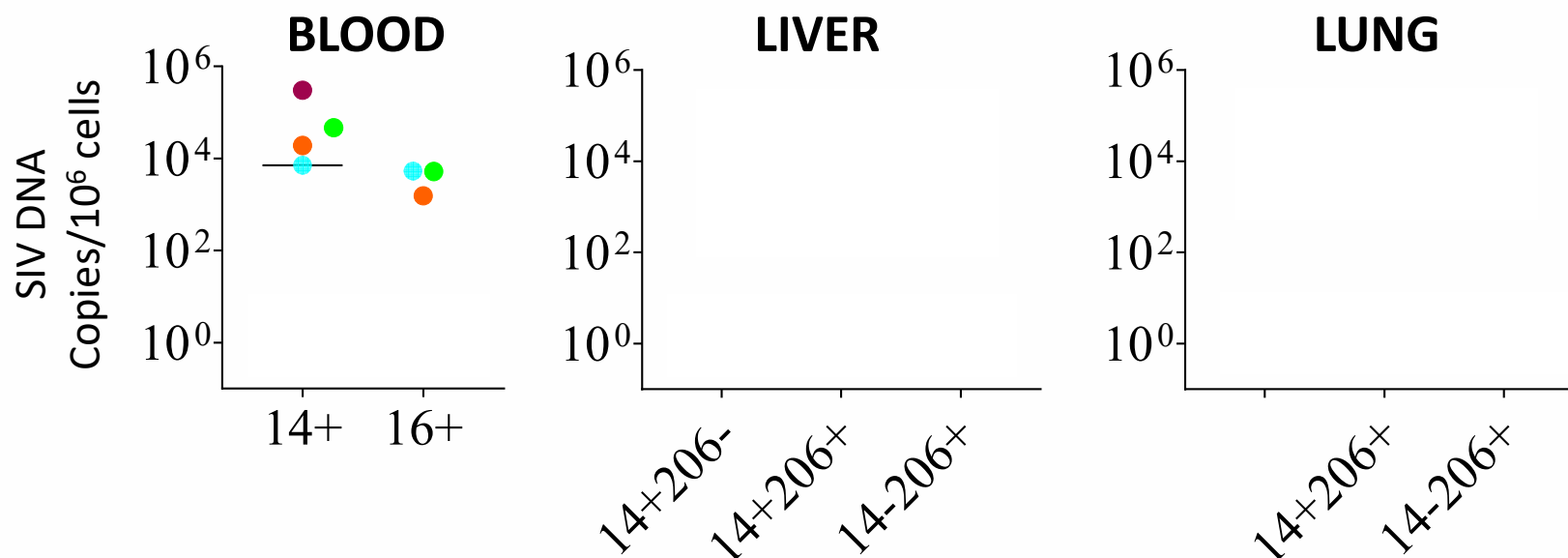
CD14 is coexpressed with CD206 on liver and lung macrophages.



Results

Viral infection of macrophages in untreated monkeys

HLA-DR+
CD11b+

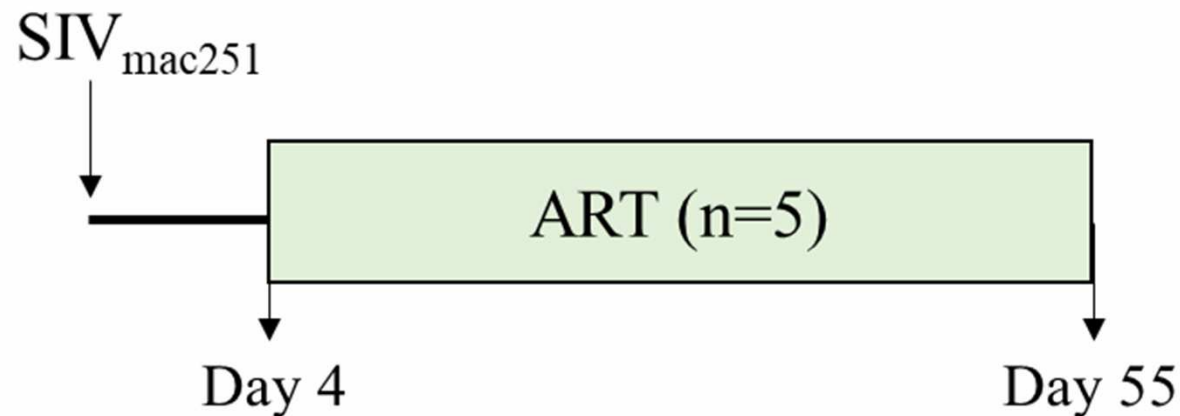


1) Individuals in whom viral DNA is detected in blood monocytes, tissue macrophage subsets contain viral DNA.

2) Tissue macrophage subsets that do not contain viral DNA correspond to individuals in whom no viral DNA was detected in blood monocytes.

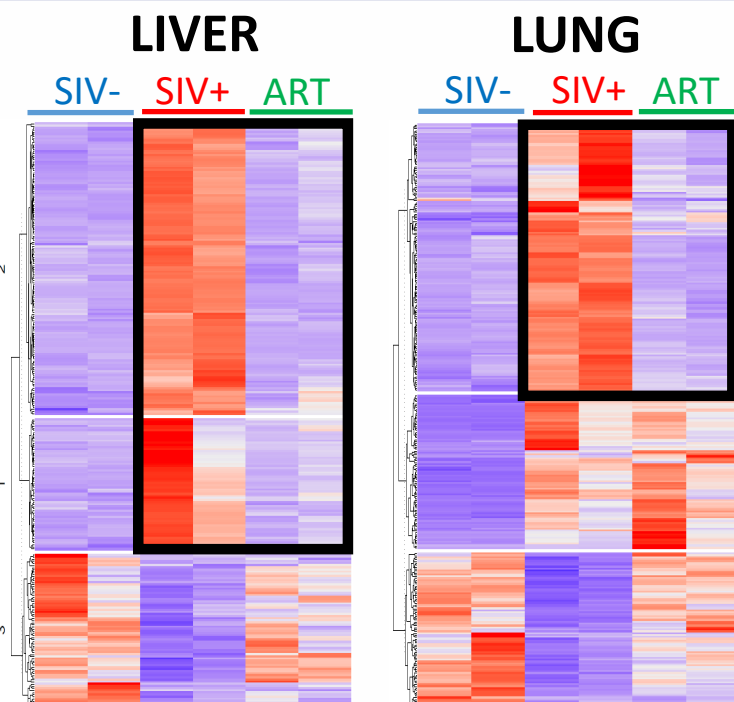


Objective 3 : Impact of early ART on viral seeding in liver and lung



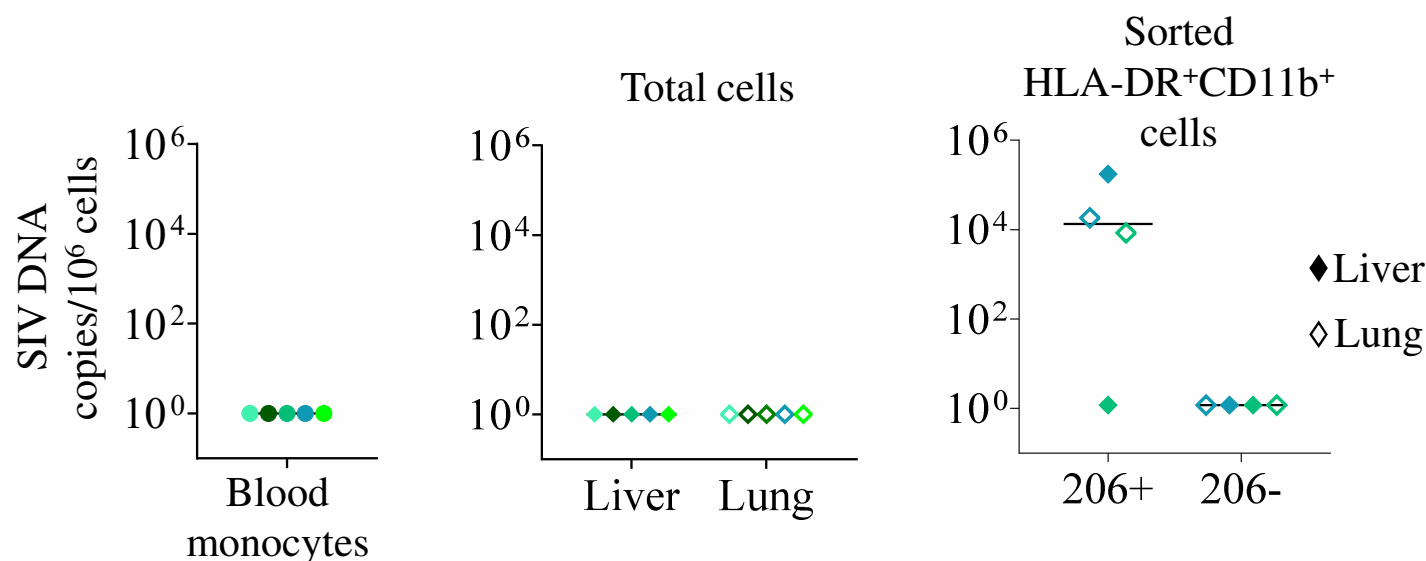


Results



↘ inflammatory response, myeloid cell, ISG transcripts.

Early ART prevents inflammation and recruitment of myeloid cells.

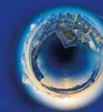


- No viral DNA detected in blood monocytes, as well as in total liver and lung
→ Early ART drastically reduces viral seeding in the liver and lung.
- HOWEVER, after cell enrichment by flow cytometry (sorting), only CD206+ cells harbor SIV DNA despite early ART.



COMMUNITY SUMMARY

- **Key question** : Does early ART prevent SIV seeding in liver and lung tissues?
- **Take-home messages** :
 - 1) Inflammation may contribute in the recruitment of myeloid cells in infected tissues.
 - 2) Presence of inflammatory macrophages (CD16+CD14+CD206+LYVE+CXCR3+) in the liver and lungs of SIV-infected monkeys.
 - 3) Early ART efficiently reduces viral seeding and inflammation, but SIV still persists in CD206+ macrophages, representing new insights on viral reservoir identification.
- **What is the next step?** To assess the contribution of liver and lung macrophages in viral rebound after ART interruption.



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