

People Living with HIV Exhibit Distinct HIV DNA Distribution in Gut Tissues Relative to Gut Damage

Malin Holm Meyer-Myklestad

MD, PhD

Norwegian Institute of Public Health, Department of Virology

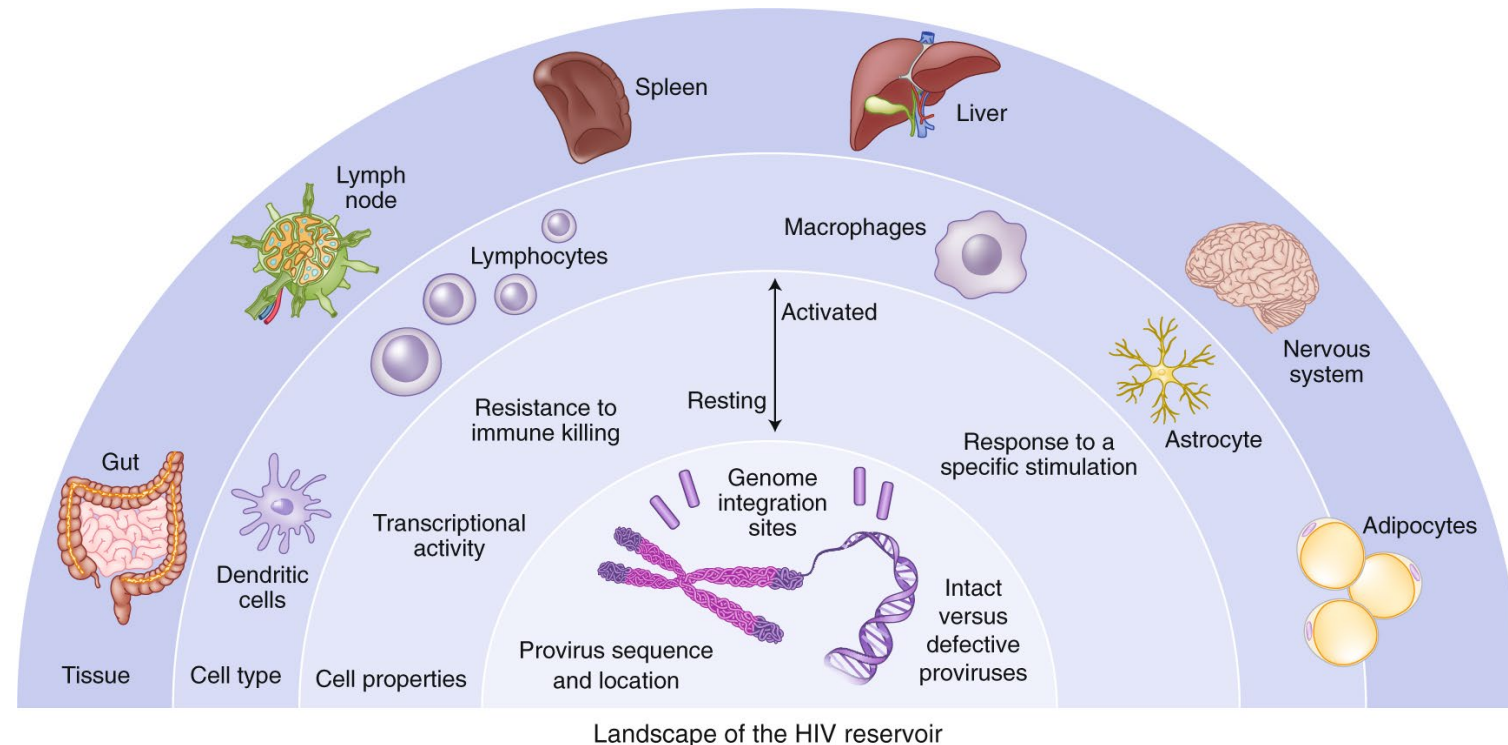
Oslo University Hospital, Department of Infectious Diseases

Outline

- Background
 - Viral reservoirs
 - Immunological nonresponders (INR)
- Method
 - Droplet digital PCR (ddPCR)
- Results
- Future plans

Viral reservoirs

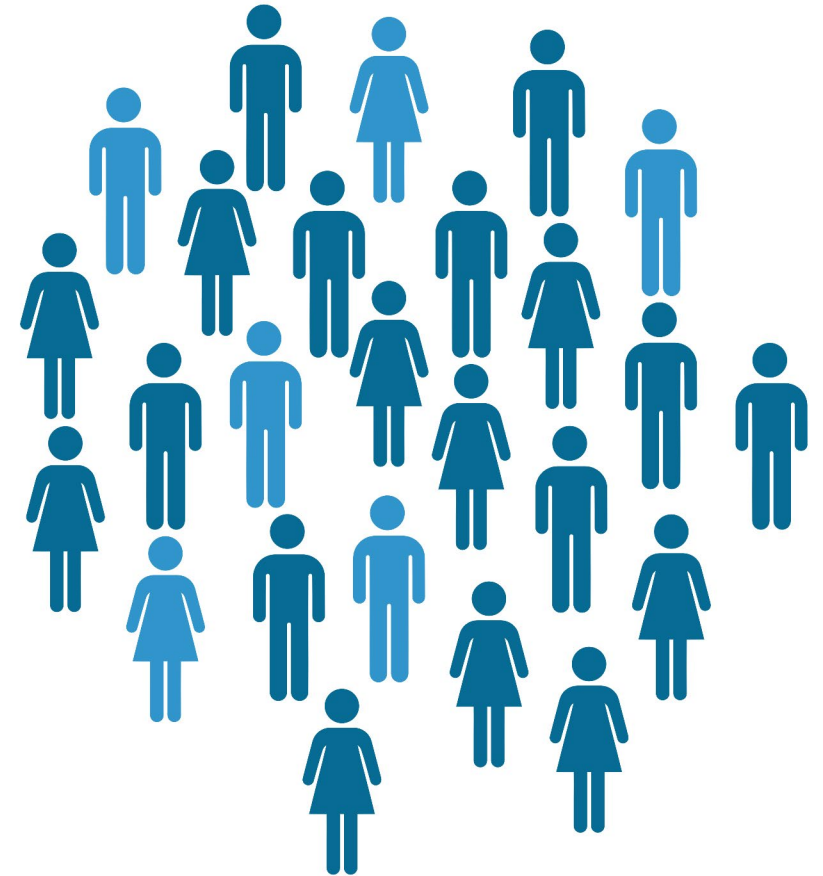
- Virus can persist in multiple forms, in multiple cells and in multiple sites
- Latently infected cells are invisible to the immune system
- A major challenge to HIV cure
- Lymph nodes and gut-associated lymph tissue are major tissue reservoirs rich in viruses and with high frequency of infected cells



Deeks, Nature Medicine 2021
Zhang, Clin Immunol. 2021.
Chun, J Infect Dis. 2002
Zaman, mBIO, 2024
Churchill, Nat Rev Microbiol. 2016

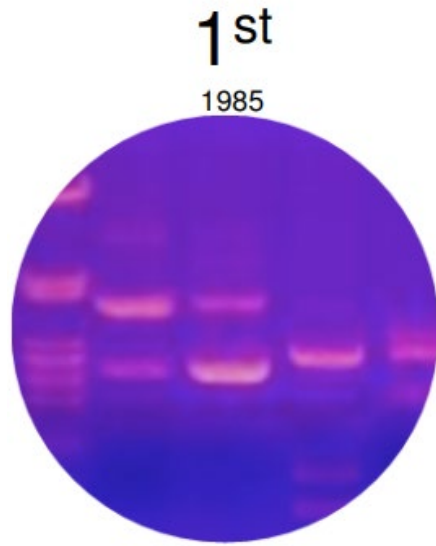
Immunological nonresponders (INR)

- CD4 < 400 cells/uL on continuous ART > 4 years
- 10-30 % of ART treated people living with HIV (PLHIV)
- Increased risk of AIDS and non-AIDS related morbidity and mortality
- Larger viral reservoirs in blood
- Increased immune activation, exhaustion and gut homing
- Etiology possibly related to a defect mucosal barrier
- Higher levels of the enterocyte damage marker iFABP



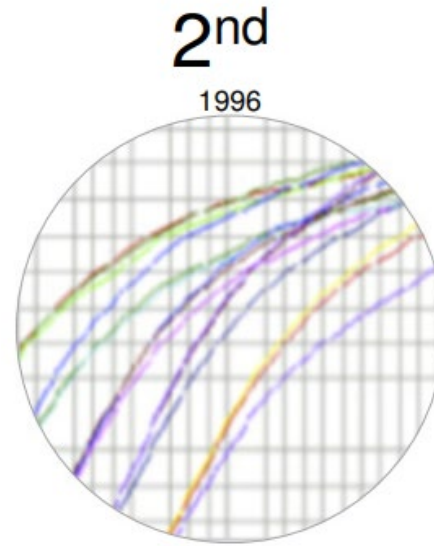
Rb-Silva, JAIDS 2019
Mutoh, Clin Infect Dis 2018
Kelly. PLoS One 2016
Stiksrud JAIDS 2016
Meyer-Myklestad. JID 2021
Lorvik Front Immunol 2021

3rd generation of PCR: Digital PCR (dPCR)



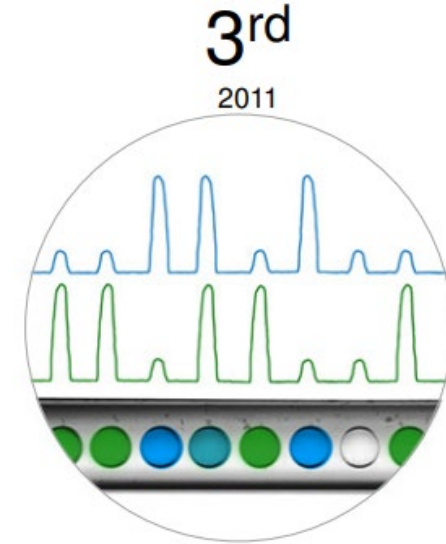
Basic PCR
Qualitative

-/+ answer



**Real-time PCR/
quantitative PCR (qPCR)**
Absolute or relative
quantitation

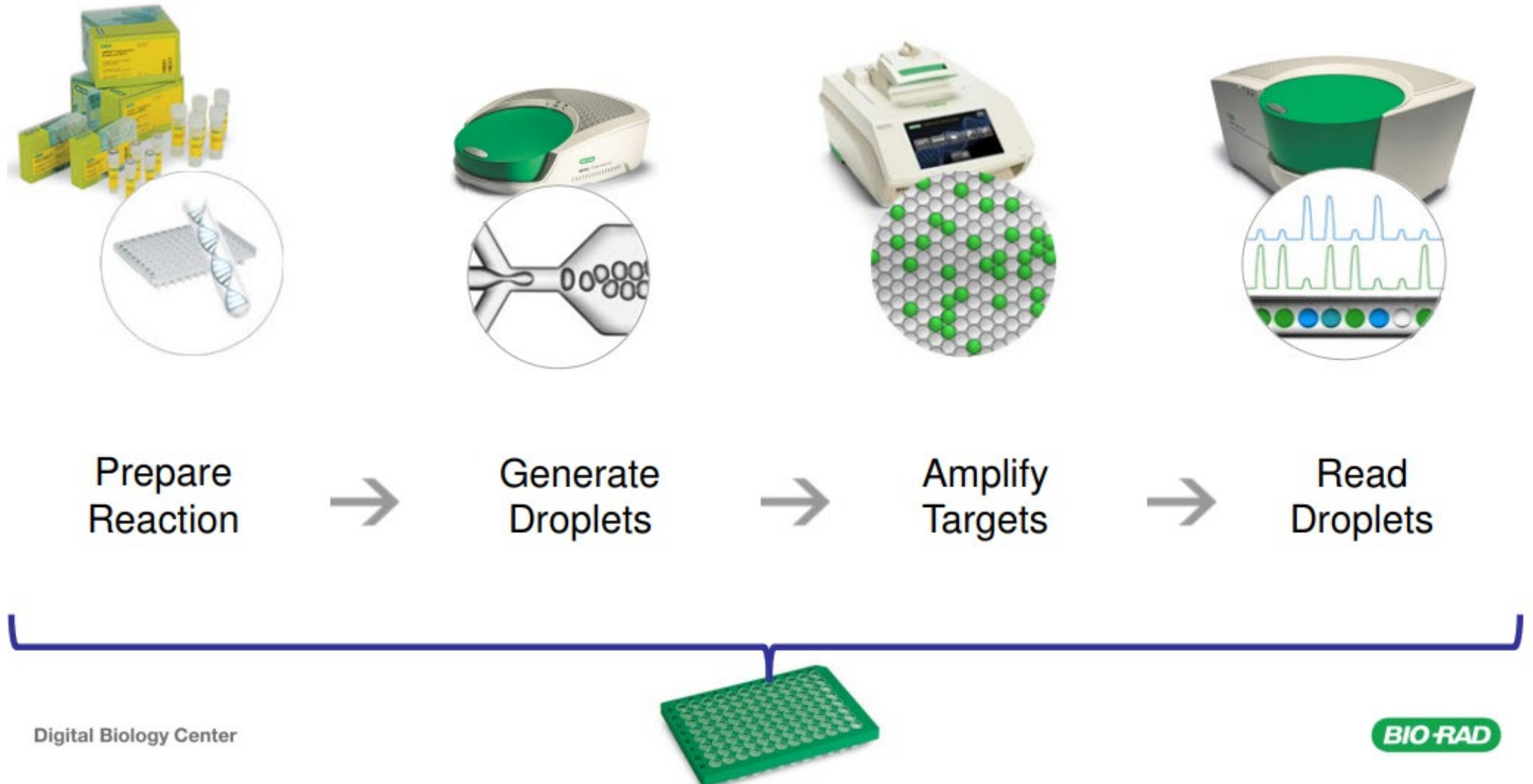
Need for standard curves
(absolute)



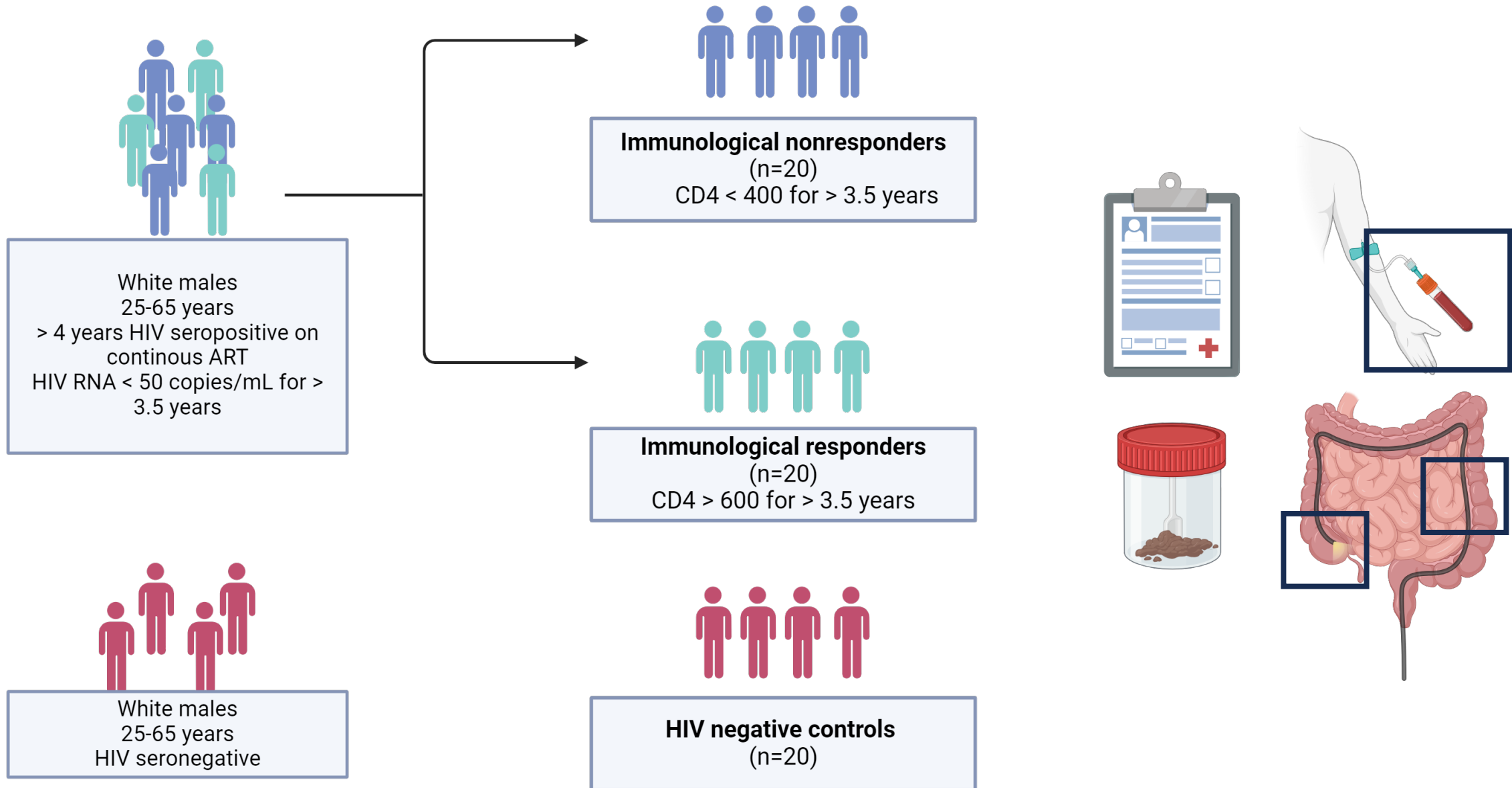
Digital (dPCR)
Absolute quantitation

No need for standard
curves, copies/ μ l

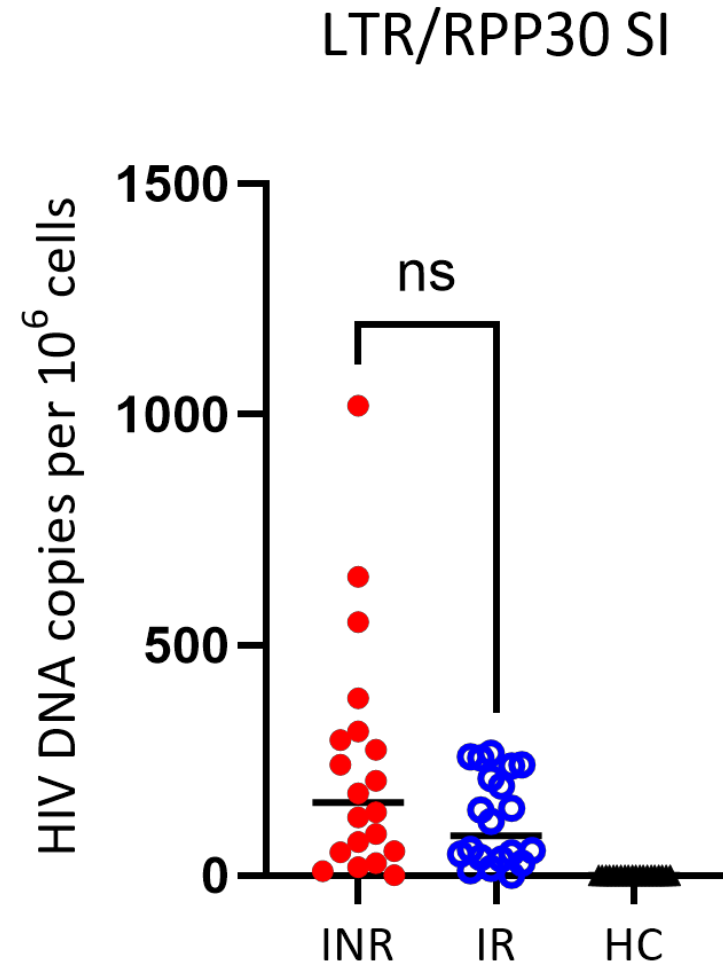
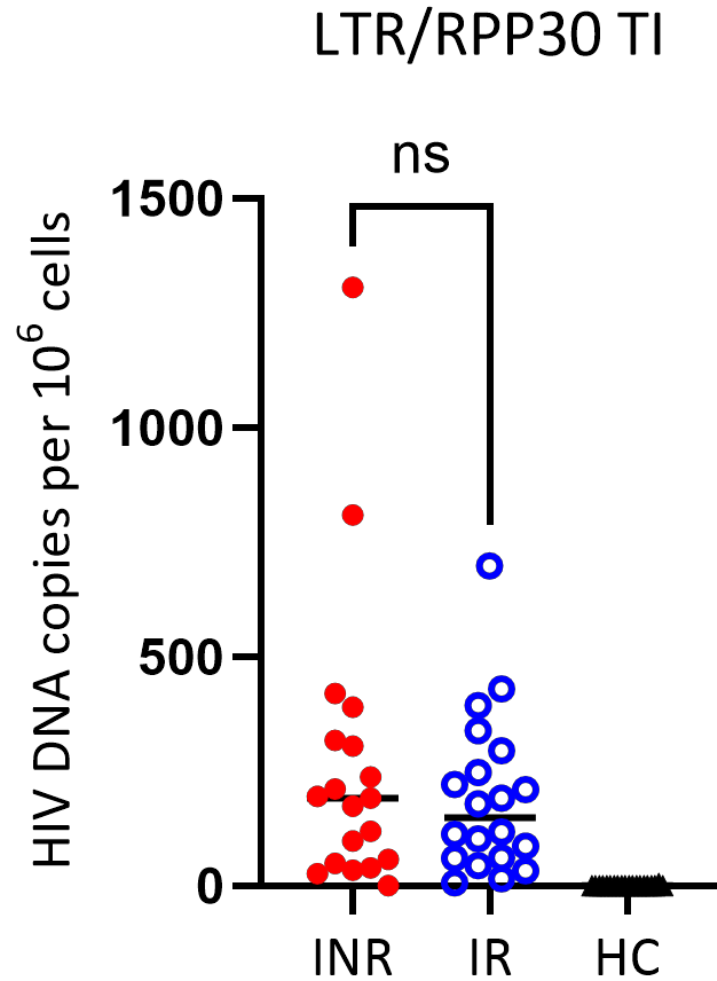
Droplet digital PCR (ddPCR) workflow



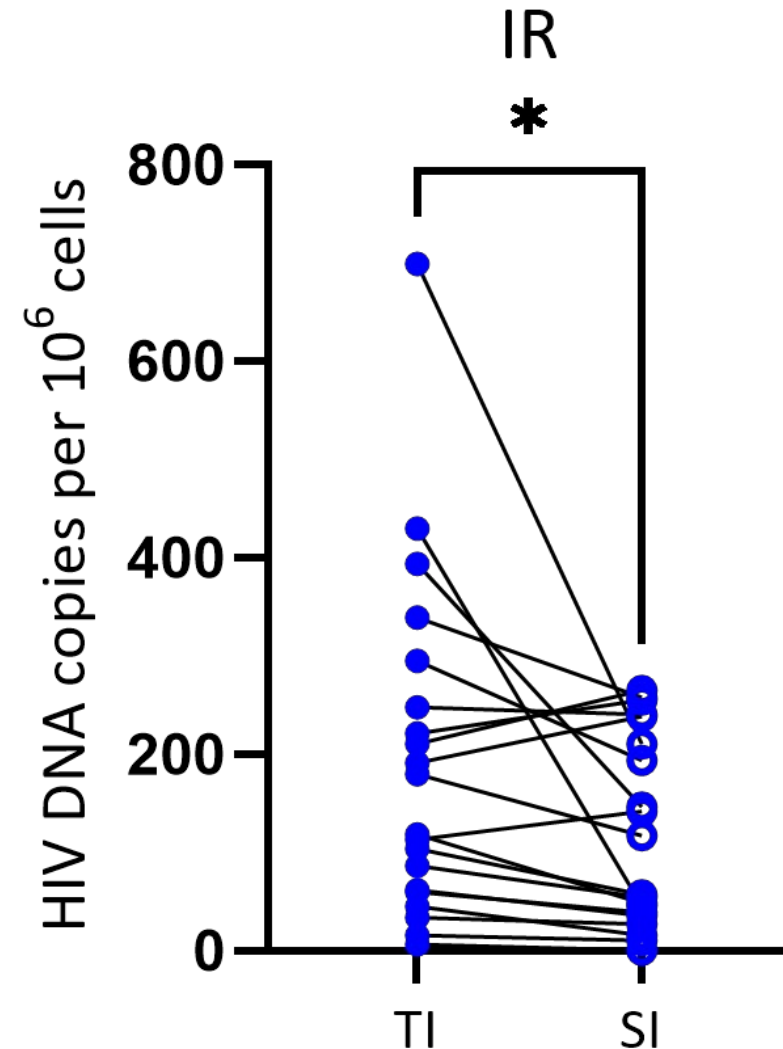
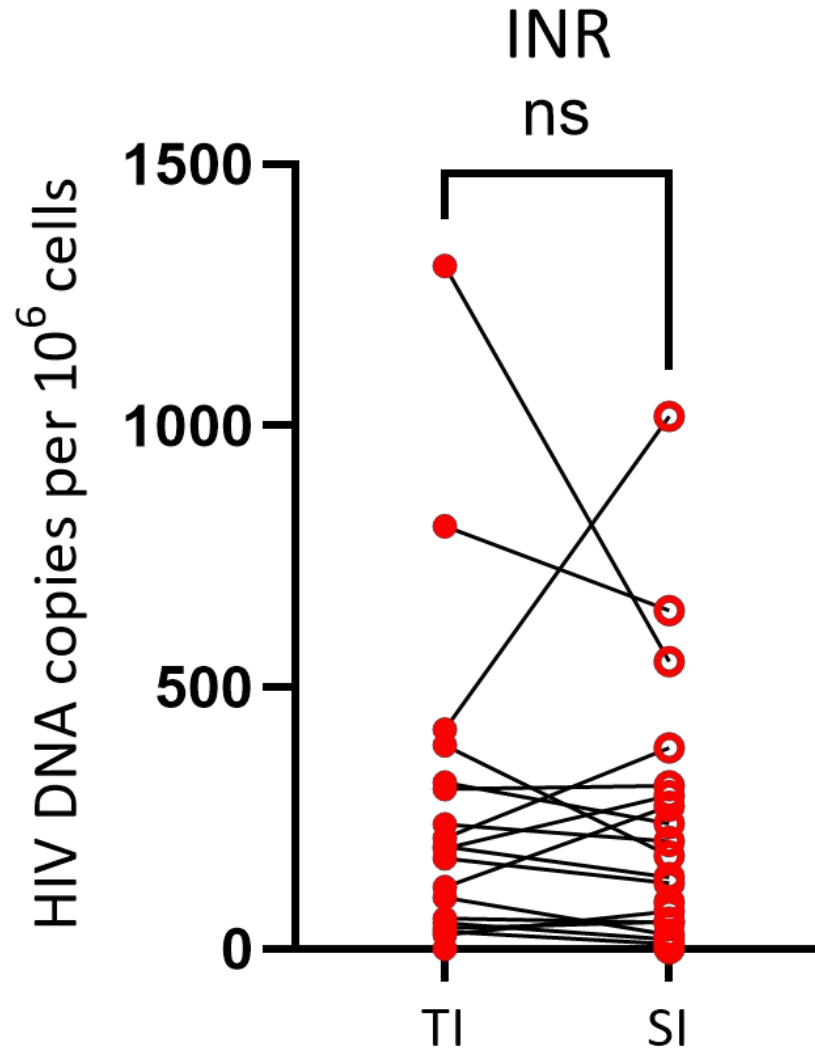
Cross sectional trail



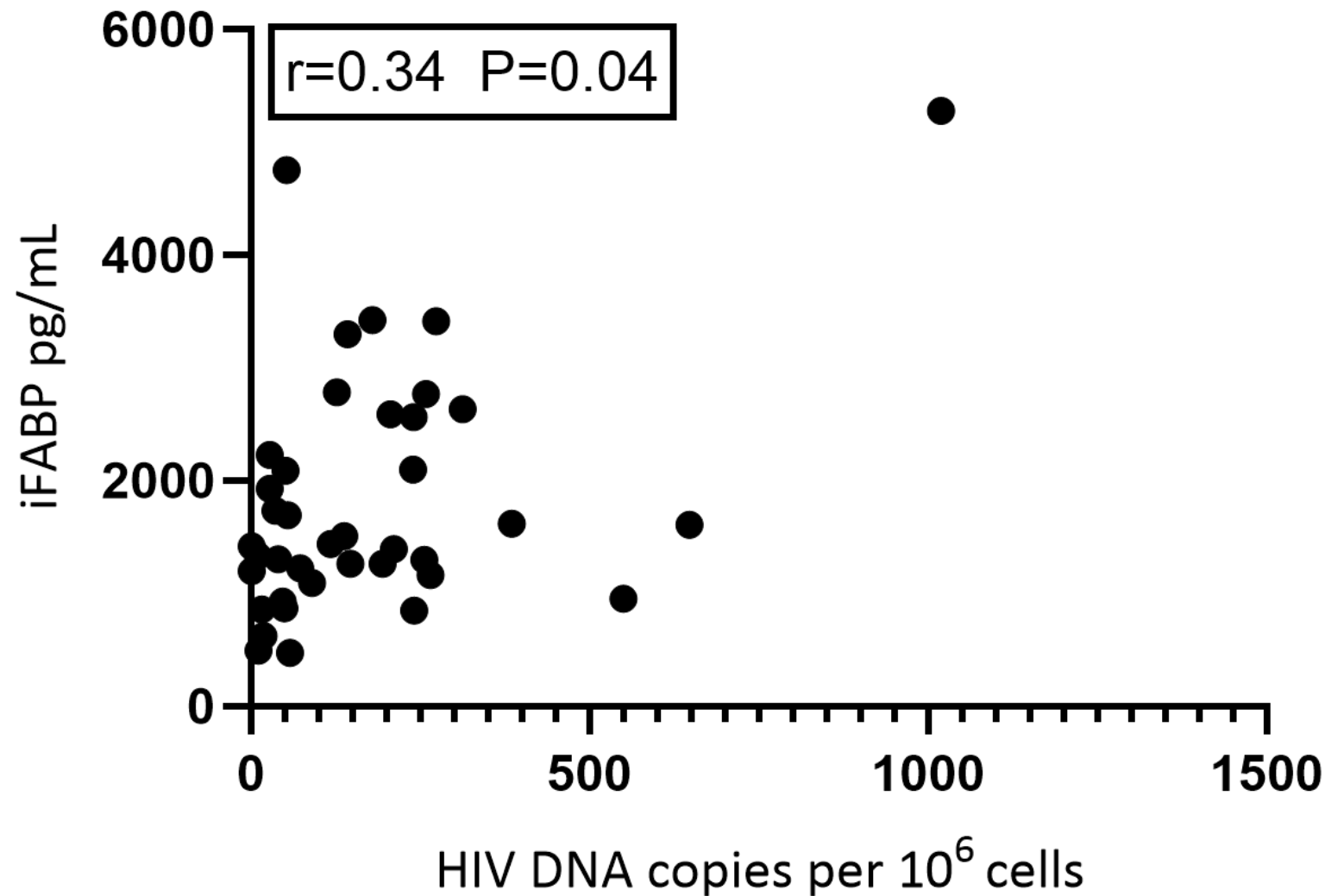
Viral reservoirs in terminal ileum and sigmoid colon



Immune responders have smaller reservoirs in colon



A possible link between mucosal damage and viral reservoirs in colon



Future plans

- Other ways of characterizing the reservoir and immunological subpopulations
 - Single nuclear RNA-sequencing (snRNAseq)
- Evaluate the role of the viral reservoir as a prognostic marker of CD4 count
 - 7-year follow-up

