Third Coast Center for AIDS Research (TC-CFAR) Viral Pathogenesis Core Workshop

Growing HIV Pathogenesis Research Across Chicago: Spatial Transcriptomics, Viral Genomics, and Data Analysis



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Bioinformatics Director, Center for Pathogen Genomics and Microbial Evolution (CPGME)

TC-CFAR Viral Pathogenesis Core Genomics

Spatial Transcriptomics

• Through TC-CFAR funding, we have developed PET-CT-Guided Spatial Transcriptomics of SIV Tissue Reservoirs.

Viral Genomics

• TC-CFAR offers HIV-1 long-read deep sequencing that makes feasible HIV single-genome, linkage-preserving, whole-genome sequencing in a more cost-effective, labor-feasible way.



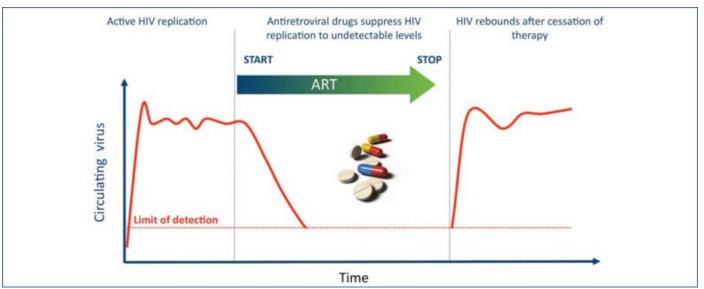
Data Analysis

 The Data Insight Group (DIG) provides consultation, navigation, training, and collaborative services to help biomedical researchers in the areas of Genomics, Molecular Evolution, and Bioinformatics.

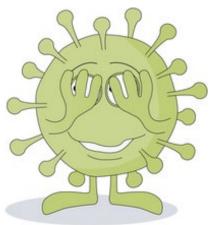


Spatial Transcriptomics

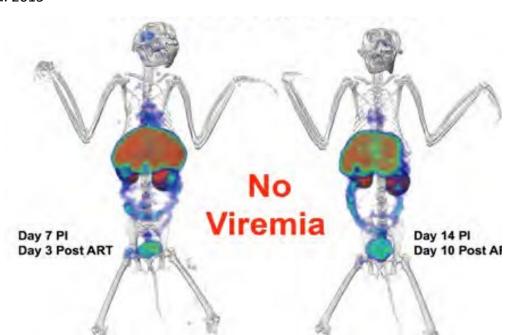
The reservoir is everywhere (and now we can find it!)



Kulpa DA, Chomont N. J Virus Erad. 2015



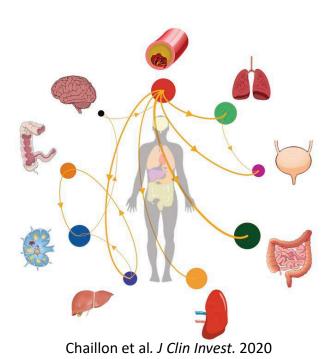
Ursula Hofer. Playing hide and seek with HIV. Nature Reviews Microbiology 14, 120 (2016)







Thomas J Hope Francois Villinger

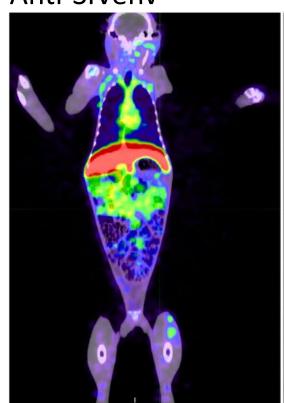


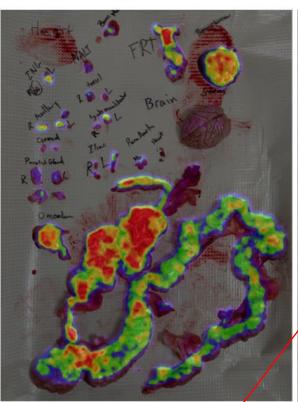


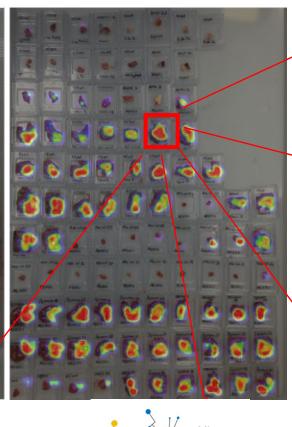
Virus-host system in SIV reservoirs

Cu⁶⁴-Fab2 Anti-SIVenv

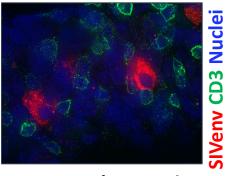
PET-CT guided necropsy



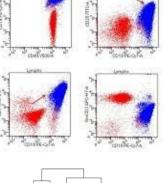


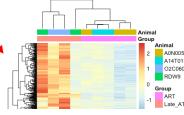


Viral diversity



Immune phenotyping





RNASeq Analysis



Spatial Transcriptomics

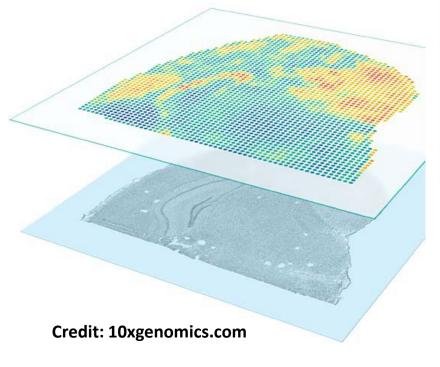


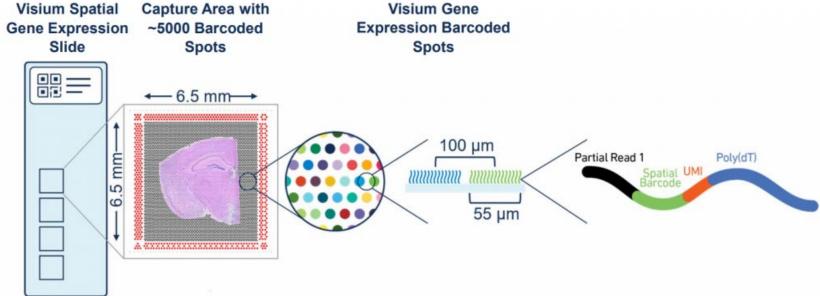
Spatial Transcriptomics

Species: Human and Mouse

Kits: Probe based or

poly-A mRNA based

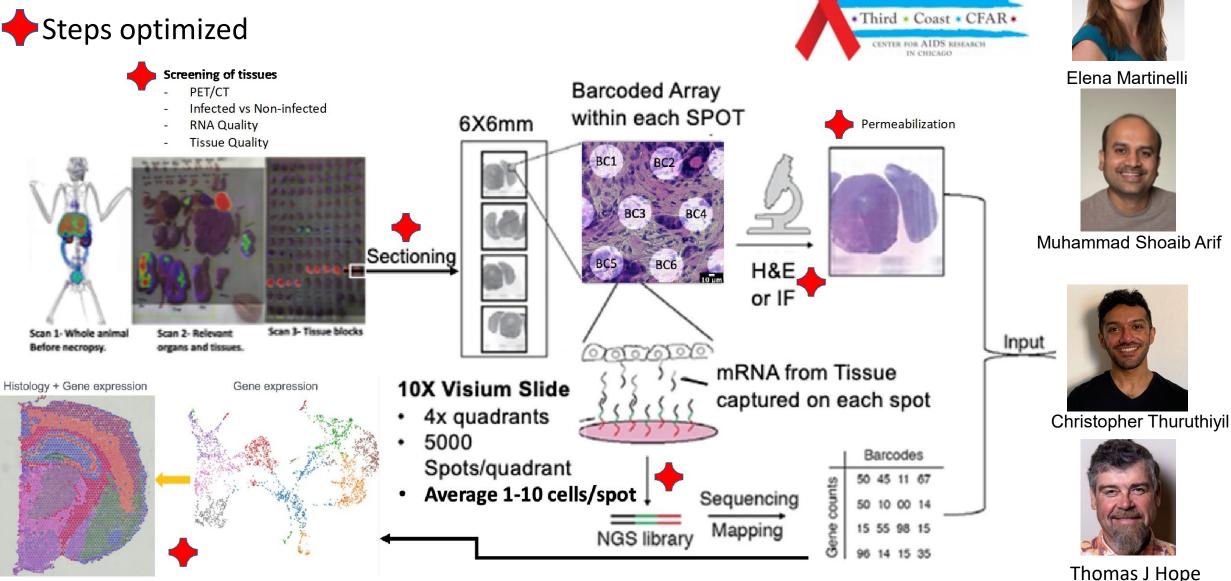




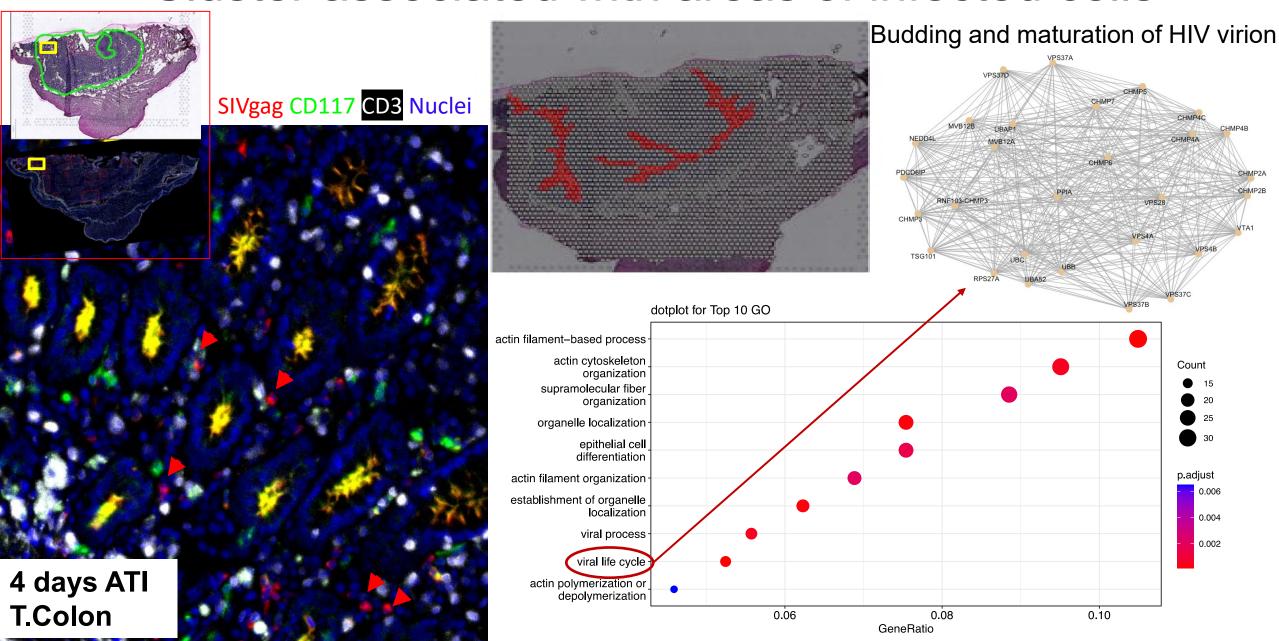
- Illumina TruSeq Read 1 (partial read 1 sequencing primer)
- 16 nt Spatial Barcode (all primers in a specific spot share the same Spatial Barcode)
- 12 nt unique molecular identifier (UMI)
- 30 nt poly(dT) sequence (captures ligation product) or poly-A mRNA

PET-CT-Guided Spatial Transcriptomics of SIV Tissue Reservoirs





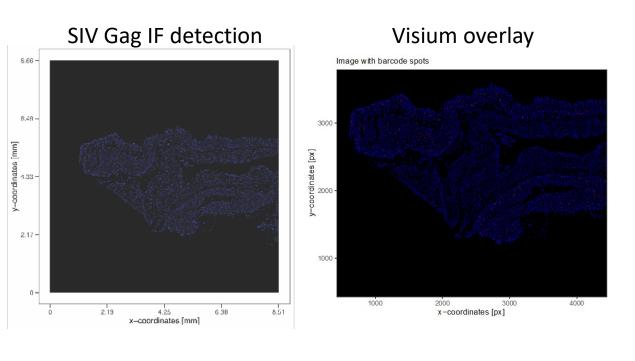
Cluster associated with areas of infected cells

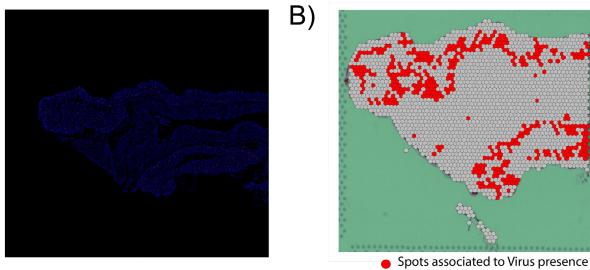


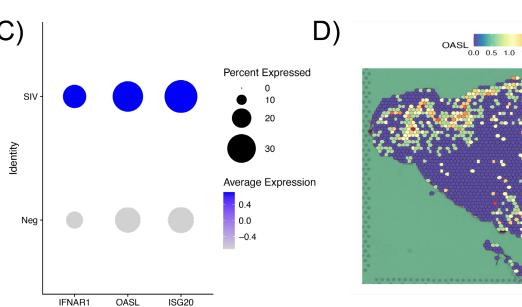
Spatial Transcriptomics associated to virus detection

A)

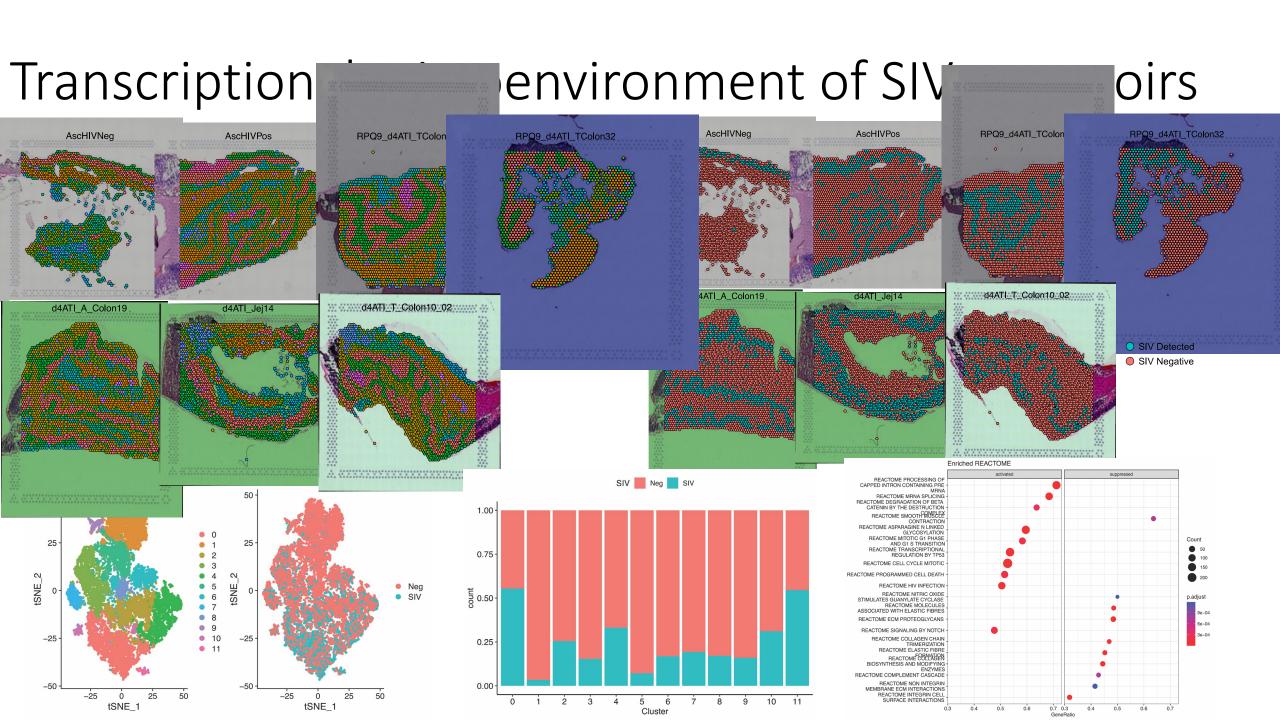
B)







Features





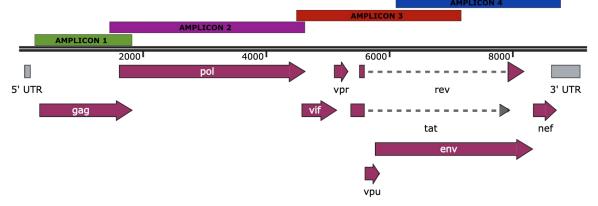
Viral Sequencing

Long-read deep sequencing

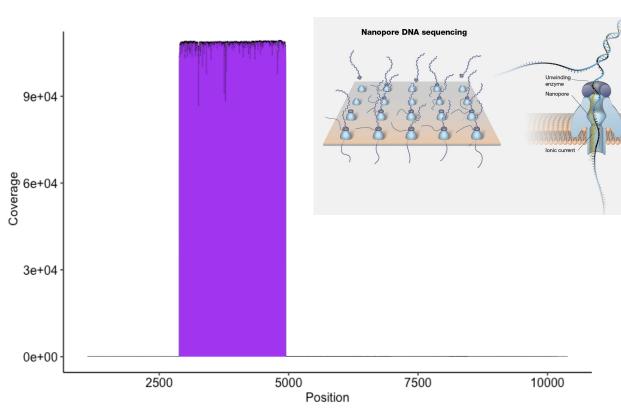
GridION Sequencer

Large-scale capacity for long-read sequencing of HIV genomes



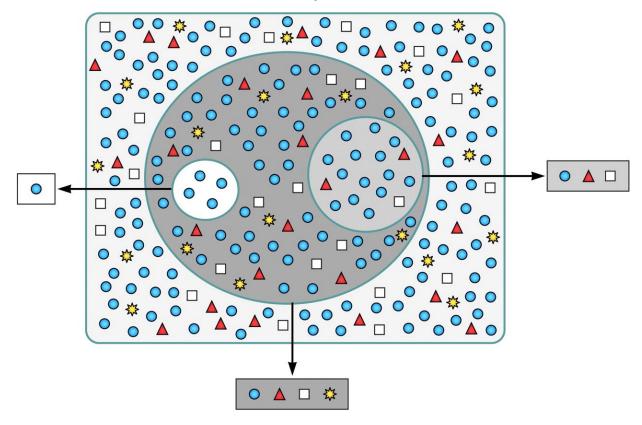


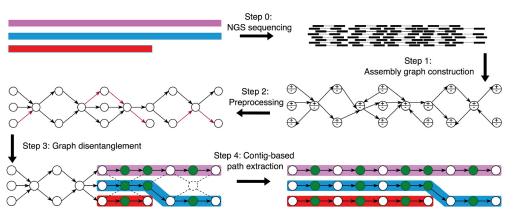


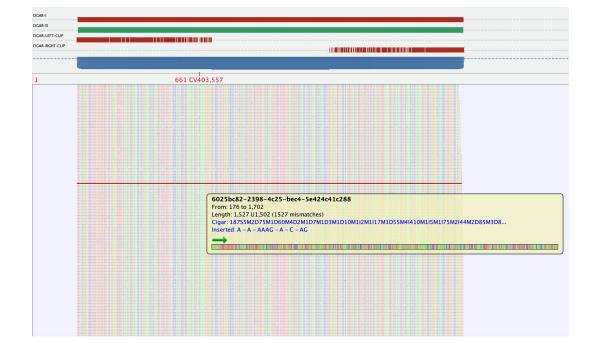


HIV-1 Quasispecies reconstruction

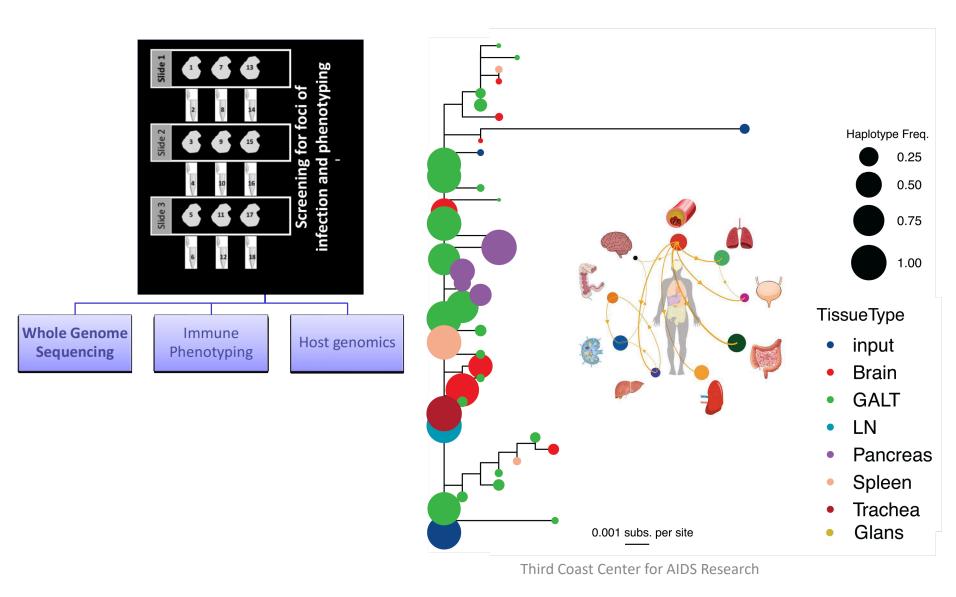
Population size may affect the evolutionary outcome

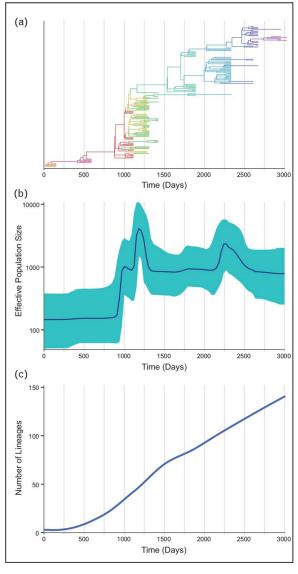






Viral Dynamics associated to reservoirs

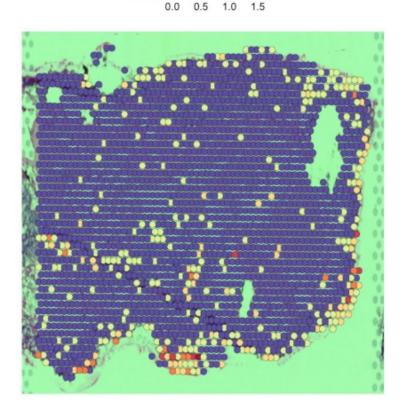




Associations between viral dynamics and spatial transcriptomics

TissueClass Ascending Colon **Descending Colon** Transverse Colon 1 Transverse Colon 2 Virus with matched spatial transcriptomics

Possible association between viral diversification and innate immunity levels.



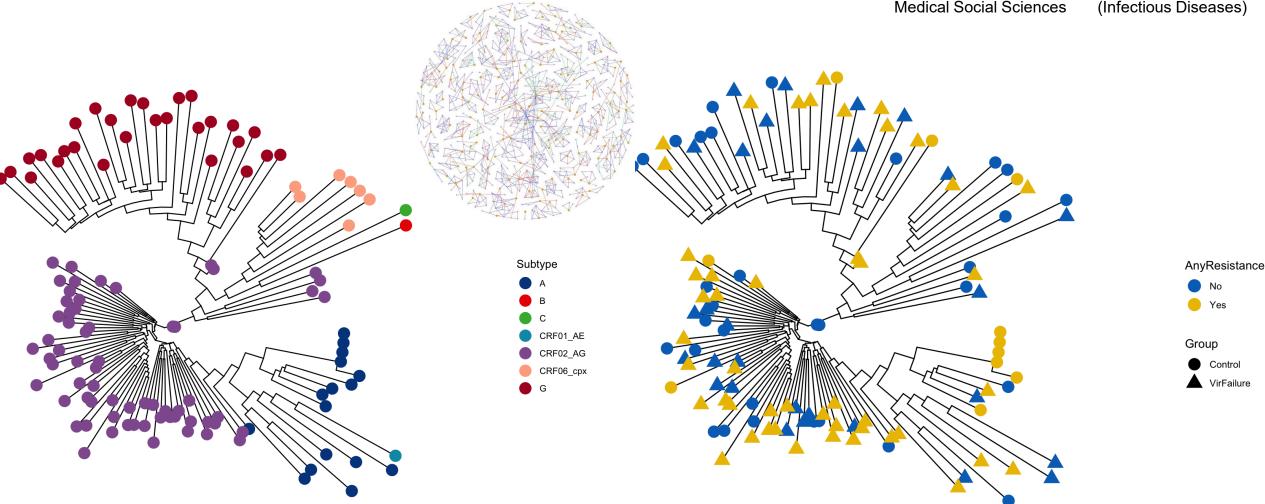
Molecular Networks and drug resistance in Nigeria



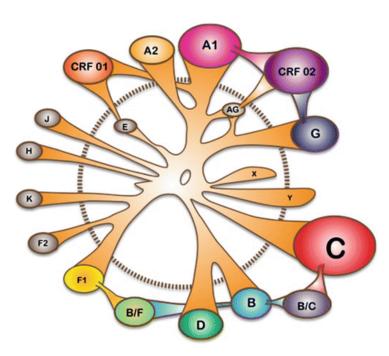
Gregory Philips II, PhD Associate Professor of Medical Social Sciences



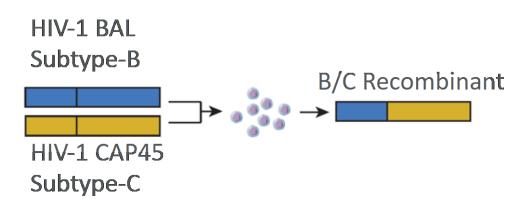
Babafemi Taiwo, MD Professor of Medicine (Infectious Diseases)

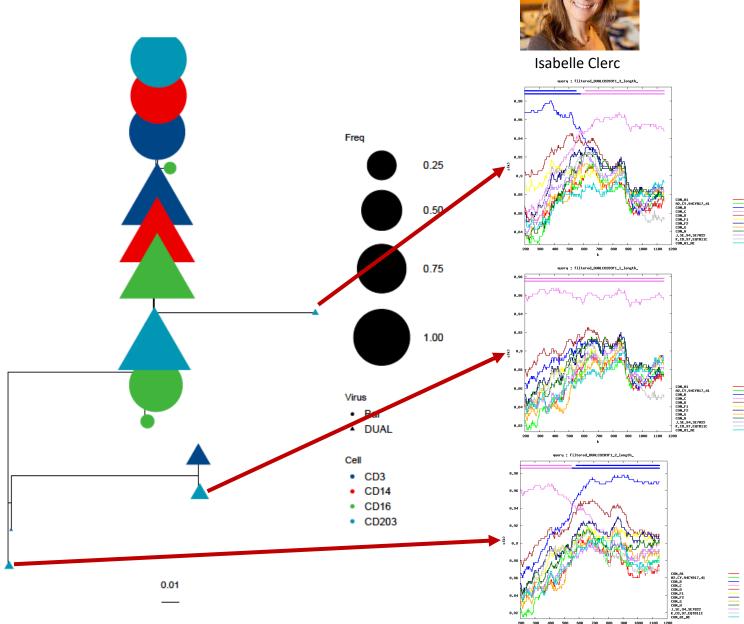


HIV-1 Recombination Detection



Abecasis, A., Vandamme, AM. (2015) Encyclopedia of AIDS.







Data Analysis

Collaborations through Data Analysis

DIG Consultation

- single-cell sequencing adaptations
- latency model -OMICs
- **Next Generation Sequencing**
- **HIV-1 Molecular Evolution**
- transcriptomics and single-cell sequencing analysis
- data modeling

Pilot / Collaborative Awards

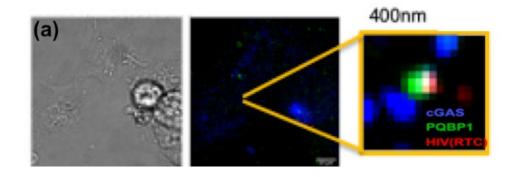
Long-term funding

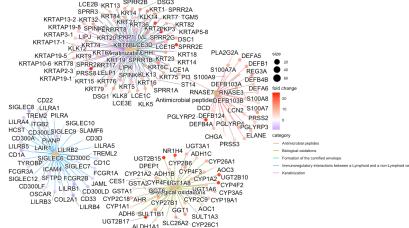


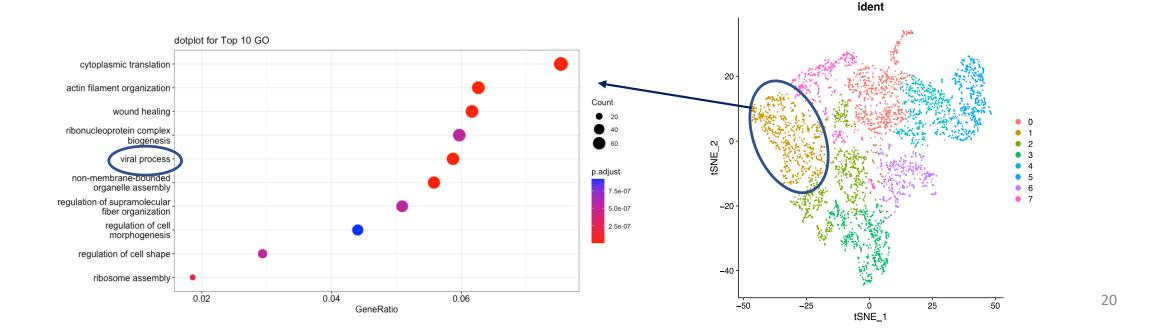
Ash, M.K.; Al-Harthi, L.; Schneider, J.R. Vaccines 2021,



Transcriptomics and single-cell analysis to study HIV-1 brain infection







Core Leadership



Core Director
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Gynecology
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Transcriptomics