POSTER # 0325

HIV POST-TREATMENT CONTROL DESPITE PLASMA VIRAL EVOLUTION AND DUAL INFECTION

Behzad Etemad[1], Golnaz Namazi[1], Ying Wen[2], Nikolaus Jilg[3], Elmira Esmaeilzadeh[1], Xin Zhang[4], Radwa Sharaf[1], Daniel MacMillan[5], Evgenia Aga[6], Ronald J. Bosch[6], Michael Bale[7], Wei Shao[7], Jeff Jacobson[8] , Ron Mitsuyasu[9], Daniel J. Skiest[10], David M. Margolis[11], Robert T. Schooley[12], Paul Volberding[13], Elizabeth Connick[14], Mary N Carrington[15], Jeffrey A. Johnson[16], Rajesh T. Gandhi[3], Zabrina L. Brumme[5], Mary F. Kearney[7], Jonathan Z. Li[1]

1. Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA ; 2.The First Affiliated Hospital, China Medical University, Shenyang, Liaoning, China; 3. Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; 4.Beijing Friendship Hospital Pinggu Campus, Capital Medical University, Beijing, China; 5.Simon Fraser University, Burnaby, BC, Canada; 6.Harvard T. H. Chan School of Public Health, Boston, MA, USA; 7.Frederick National Laboratory for Cancer Research, Frederick, MD, USA; 8.Case Western Reserve University, Cleveland, OH, USA; 9.David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA; 10.University of Massachusetts Medical School-Bay State, Springfield, MA, USA; 11.School of Medicine and UNC HIV Cure Center, UNC Chapel Hill School of Medicine, Chapel Hill, NC, USA; 12.Department of Medicine, Division of Infectious Disease and Global Public Health, University of California San Diego, La Jolla, CA, USA; 13.School of Medicine, University of California, San Francisco, CA, USA; 14.Department of Medicine and Cancer Center, School of Medicine, University of Arizona, Tucson, AZ, USA; 15.Cancer and Inflammation Program, Laboratory of Experimental Immunology, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, Frederick, MD, USA and Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, USA; 16.Centers for Disease Control and Prevention, Atlanta, GA, USA

Background

- HIV post-treatment controllers (PTCs) are individuals who can maintain low levels of viremia after ART discontinuation.
- Viral sequence analysis may provide insight into mechanism of viral control and escape.
- Understanding the mechanisms of HIV control has implications for the design of novel strategies for HIV remission.

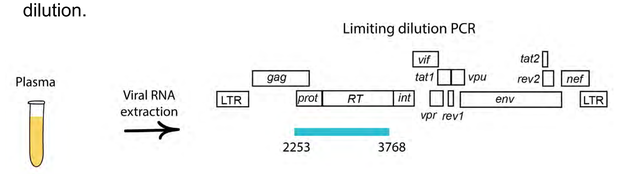
Objectives

- **To assess for evidence of viral evolution in PTCs and post-treatment non-controllers (NCs)**

Methods

Data Sources, Study, and Participant Selection

- We obtained >1200 single-genome plasma sequences from 20 PTC and 13 NC participants from 5 ACTG ATI studies.
- Nested ProRT PCR was performed on plasma viral RNA at limited dilution.



Sequence and data analysis:

- ClustalW and Neighbor-Joining Tree (NJT)
- Viral diversity by average pairwise distance (APD)
- Viral divergence by root-to-tip distance
- Presence of HLA-escape mutations
- Population structure by the panmixia test
- Microbe trace analysis for intra-patient diversity

Results

Figure 1:Example of HIV Sequence Evolution in a PTC

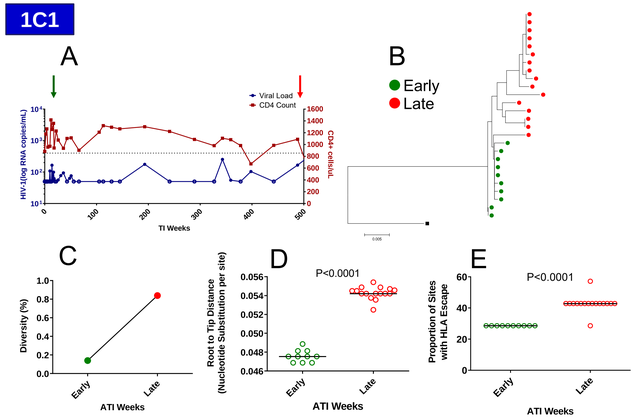
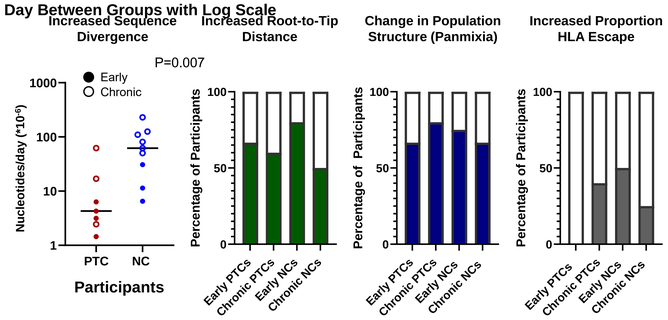
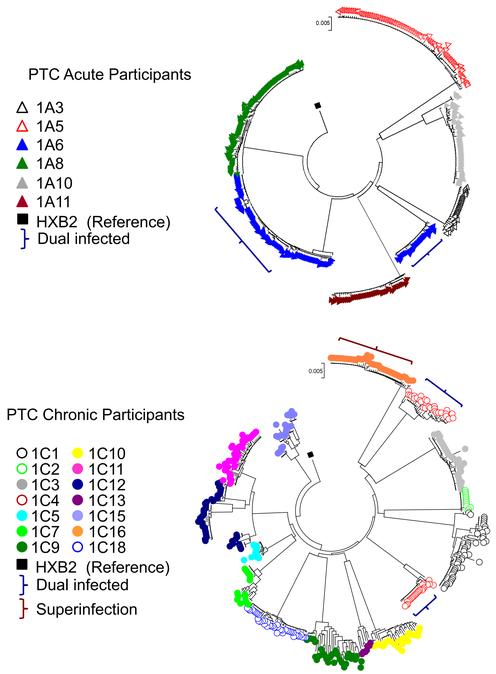


Figure 2: Evidence of HIV Sequence Evolution in PTCs and NCs



- PTCs had a median 96 weeks of documented viral control
- Increasing viral diversification and evolution detected in most PTCs despite low levels of viremia
- Increased sequence divergence and root-to-tip distance
- Changes in population structure by the panmixia test
- HLA-escape mutations were commonly detected in PTCs and NCs and a subset increased in proportion HLA-escape.

Figure 3: Neighbor-Joining Trees for PTCs and NCs



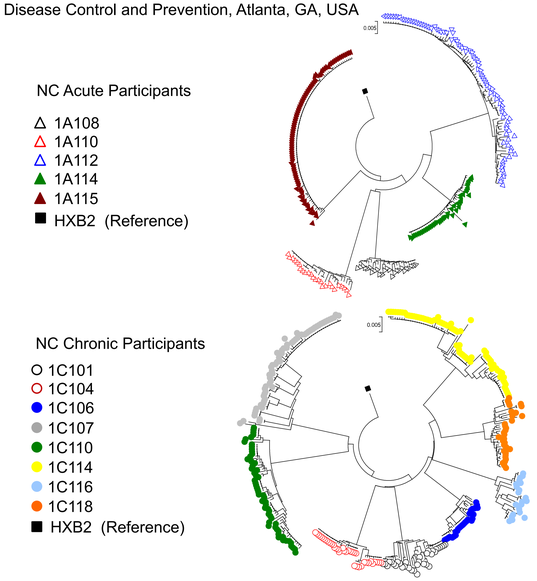


Figure 4: Post-Treatment Control can be Maintained Despite Dual or Superinfection

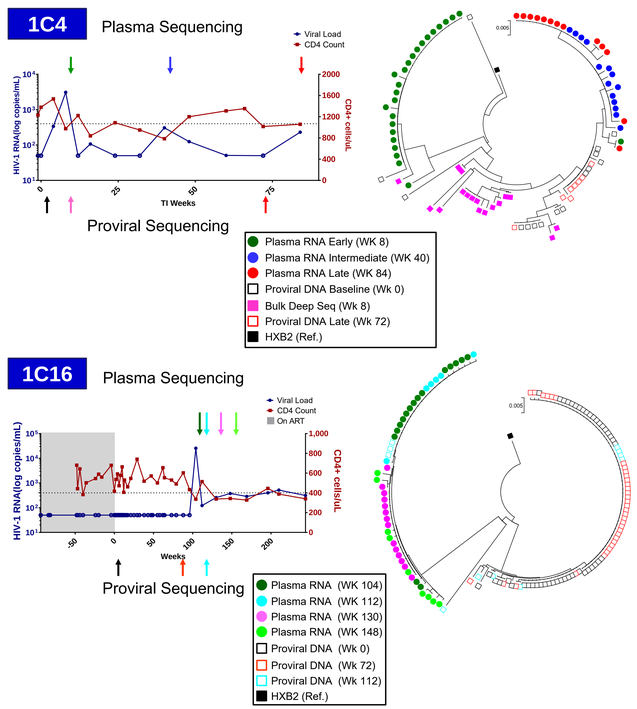
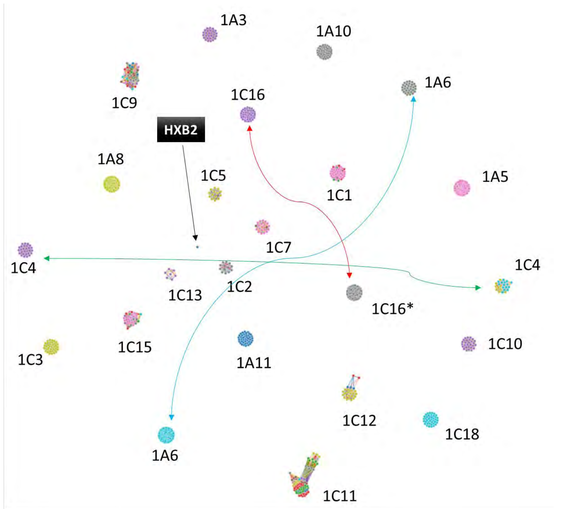


Figure 5: Microbe Trace Analysis for all PTC Participants



- Microbe trace analysis shows intra-patient diversity in dual infected PTC participants (1A6, 1C4, 1C16).
  ∗ Indicates proviral sequences

Conclusions

- Despite low-levels of HIV viremia, we were able to obtain >1200 HIV plasma sequences from HIV PTCs and NCs.
- PTCs exhibit sustained HIV remission despite evidence of slow plasma viral diversification and evolution.
- Increasing frequency of HLA-escape mutations in a subset of PTCs could indicate presence of some T cell-mediated immune pressure.
- The detection of dual HIV infection and superinfection in a subset of PTCs suggest the presence of an antiviral response that can control a highly diverse viral population.

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