PrEP Seroconversion-Segmental Hair Analysis for Unraveling Timing of Viral Resistance

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BACKGROUND

- PrEP failure can result from either low adherence or acquisition of resistant virus
- We describe a case of HIV acquisition on PrEP with resistant virus but 100% self-reported adherence, suggesting an algorithm to unravel such cases

CASE

- 44-year-old MSM in Texas started daily TDF/FTC PrEP in 12/2017 after a negative fourth-generation Ag/Ab HIV test; quarterly testing thereafter with negative HIV tests
- Early June 2019, presented with headache, abdominal pain, sore throat, →HIV Ag/Ab test reactive, but HIV-1/HIV-2 antibody differentiation assay negative
- HIV RNA level returned as 3,100,687 copies/mL
- Genotype: M184V, K70N mutations in RT, conferring emtricitabine and low-level tenofovir resistance
- Participant enrolled in the UCSF SeroPrEP Study to investigate etiology of seroconversion on PrEP despite high self-reported adherence

METHODS

- Cumulative PrEP adherence assessed via TFV-DP levels in dried blood spots and TFV levels in hair using segmental hair analysis
- Single genome sequencing (SGS) used to evaluate timing of infection to provide evidence on whether resistance was transmitted or evolved (on 2-drug PrEP with active HIV)

Objective adherence metrics that look back over time combined with single genome sequencing can help unravel the etiology of seroconversion on PrEP.

RESULTS

- TFV-DP levels in DBS consistent with estimated daily adherence over preceding 6-8 weeks
- Segmental hair TFV levels consistent with ~6x weekly adherence over the prior 2 months
- Single Genome Sequencing identified homogenous viral population consistent with acute infection

CONCLUSIONS

- Acquisition of drug-resistant virus despite high adherence (measured objectively) has been described in 5 prior cases
- We describe the second time where SGS was used to confirm transmission of resistant virus
- PrEP seroconversion due to transmitted resistance is rare (with public health implications), despite increasing PrEP use worldwide
- Improving population-level viral suppression should make such events rarer still

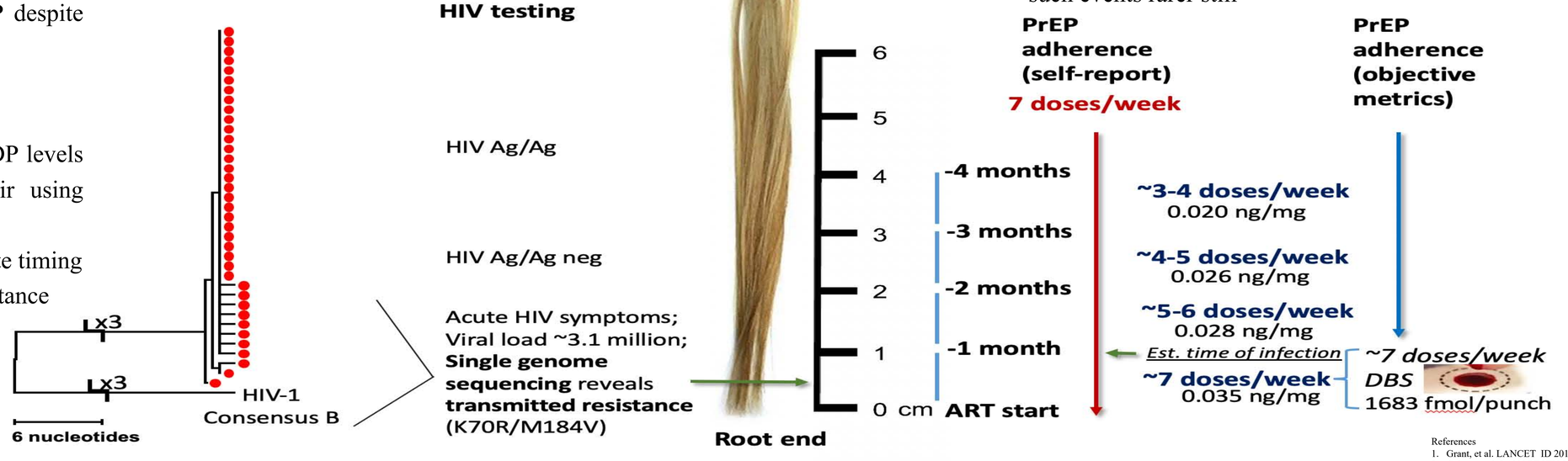


Figure: Illustration of adherence patterns and single genome sequencing in this case, unraveling that patient likely acquired a transmitted drug-resistant HIV virus while on PrEP with high adherence. PrEP: pre-exposure prophylaxis; ART: Antiretroviral Therapy

References
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