NEAR REAL-TIME IDENTIFICATION OF RECENT HIV INFECTION BY PID-NGS IN NORTH CAROLINA

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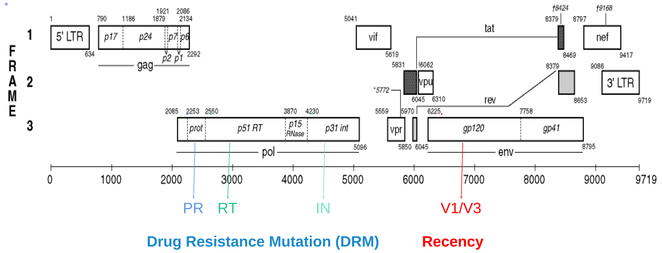
BACKGROUND

- The identification of recent (incident) HIV-1 infections among people with newly diagnosed infections is important to both tailoring and assessing the impact of HIV-1 prevention strategies.

We developed a Multiplexed Primer ID-Next Gen Sequencing (MPID-NGS) approach to identify recent infections by measuring the intra-host viral diversity over multiple regions of the HIV-1 genome. Here we summarize the field implementation of this approach to identify recent infections, drug resistance mutations (DRMs) and phylogenetically linked clusters among persons newly diagnosed by the North Carolina State Laboratory of Public Health (NC SLPH) in 2018.

METHODS

- All **HIV-1** specimens from persons **with new diagnoses**
- **MPID-NGS libraries** were constructed covering the coding regions for protease (PR), reverse transcriptase (RT), integrase (IN), and the V1 to V3 region of the env gene from diagnostic samples of HIV-positive sera. The MiSeq platform was used for sequencing.
- The **TCS-DR pipeline** was used for bioinformatics analysis and to identify DRMs.
- Recent infections were defined as within **nine months of transmission**, using average and distribution of **pairwise diversity of RT and V1V3**. (Dennis, et al. JID 2018)



Drug Resistance Mutation (DRM)
Recency (RT)
Clustering (RT consensus)

Recency
Coreceptor usage
Other phylogenetic analysis

All-in-one platform to monitor **HIV-1 recency, DRMs** and **transmission clusters** in near real-time.

Recent HIV-1 infection (**within 9 month**) in **35%** of new diagnosis in NC 2018.

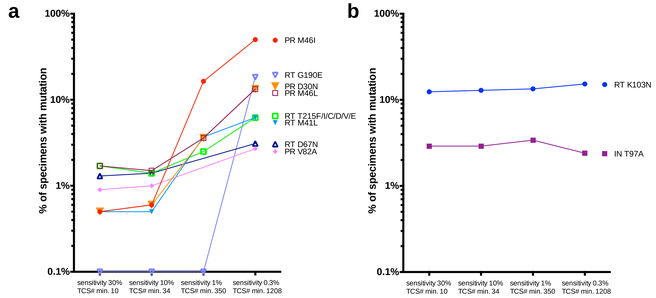
Clinically important **DRMs** low.

Recent infections more likely **clustered**.

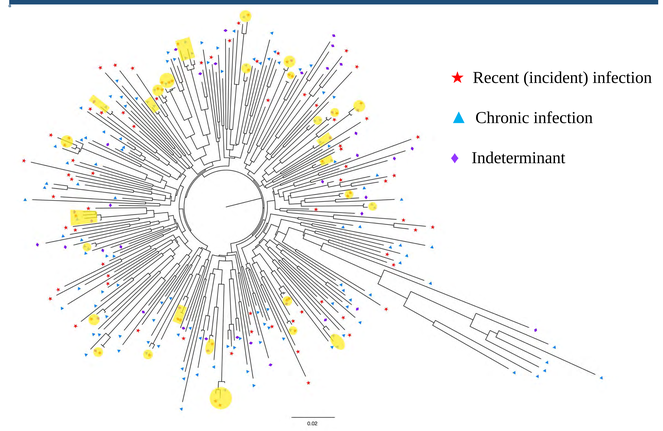
RESULTS

- HIV+ samples from 294 individuals were subjected to sequencing. **268** (91.2%) were successfully sequenced. Overall, recent infection was identified in **94** people (**35%**).
- Multi-variant regression analysis showed that **people younger than 30 years old** and **PWID** were more likely to be diagnosed as **recent infection** with adjusted OR of **2.17** (95% CI 1.21-3.98, p=0.01) and **5.31** (95% CI 1.18-37.59, p=0.047), respectively.
- The **RT region** had more **DRMs** than the PR or IN regions, and **K103N** was the most common transmitted DRM (approximately 10% of samples). RT mutations M184V, K65R and major IN DRMs were rarely identified.
- We found a total of **28 clusters** using a similarity cut-off at 1% among the newly diagnosed individuals. Persons with **recent infection** were **more likely to be cluster members** compared to those with chronic infections (32% vs. 18% in clusters, p = 0.026).

Selected SDRMs identified using different sensitivity cut-offs.



ML tree of RT individual consensus sequences for 268 newly diagnosed patients. Transmission clusters were highlighted in yellow.



CONCLUSIONS

- We demonstrate the **rapid identification** of recent infection and pre-treatment drug resistance coupled with cluster analysis that will allow prioritization of linkage to care, treatment and prevention interventions to those at highest risk of onward transmission and their at-risk partners within a useful time frame.
- **Monitoring recency** can also serve as a measure for the true HIV-1 incidence rate to **evaluate prevention efforts** over successive years.

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