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Poster presentation

P20-15. Evaluation of HIV-1 subtype B acute envelope-expressing infectious molecular clones

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Background

Understanding the biological phenotype of transmitted HIV isolates may be critical to the design of effective vaccine responses. As such, infectious molecular clones (IMCs) containing subtype B envelope (env) sequences derived from CHAVI acute infection studies (Keele et al., 2008, PNAS) were evaluated for cellular and tissue tropism.

Methods

Individual viruses (20) were evaluated for differential tropism in cellular assays (PBMC, monocyte-derived macrophages, PM1, TZM-bl cells, dendritic cells and dendritic cell-T cell trans-infection) and explant tissue assays, (ectocervix, penile glans, rectal and tonsil). Relative replication of each virus among the different models was assessed by infecting with virus for two hours, washing and measuring p24 release in supernatant over time.

Results

There were variable levels of replication by the acute env clones. Moderate to high levels of replication for all clones were seen in PBMC and T cells and there was preferential replication in rectal tissue, possibly reflective of the higher number of activated CD4+ CCR5+ T cells. Low levels, or inefficient replication were seen in macrophages and dendritic cells and there was poor transmission of env-IMC virus from DC (monocyte-derived and tissue) to T cells by trans-infection, suggesting a predominant T cell tropism. All clones replicated equally in cervix and tonsil tissues, suggesting that T cells are the dominant population for primary infection.

Conclusion

T cell tropism represents the dominant selected biological phenotype of transmitted/founder virus, and preferential infection of rectal tissue may reflect target cell tropism. Ongoing evaluation will compare the isogenic molecular clones expressing different envs in cis to matched full-length IMC to determine additional influence of non-envelope sequences.