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Primary Human Connective Tissue Mast Cells are Not a Reservoir for HIV

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INTRODUCTION

Human Immunodeficiency Virus (HIV) is the virus that causes Acquired Immune Deficiency Syndrome (AIDS). While Highly Active Anti-Retroviral Treatment (HAART) medications have been efficacious in suppressing viral replication, once it is discontinued virus emerges from cellular reservoirs [1]. However, it is not clear what cell types the virus uses as latent cellular reservoirs. Identifying the cellular reservoir in which HIV invades and eludes the immune system is of the utmost importance as this will facilitate new strategies to potentially target and kill those infected cells [2].

DESCRIPTION

Mast cells are ubiquitously expressed cells residing in tissue and mast cell progenitors can be infected with HIV, which can lead to a latent reservoir in tissue in humans [3]. Other studies using mast cell-like cell lines or mast cells derived from progenitor cells in the blood can be infected. Most recently, mast cells from gastrointestinal mucosa were shown to be susceptible to HIV infection while other studies found no evidence of active replication in mast cells.

To our knowledge no studies have examined if human Connective Tissue Mast Cells (MC_{TC}) serve as a reservoir for HIV vial latency [4]. Given that MCTC mast cells are one of the first immune cells that HIV encounters *in vivo*, we hypothesized they could be infected by HIV following FcεRI or non-FcεRI receptor dependent challenge with various secretagogues and serve as a latent reservoir for HIV.

To test this hypothesis MC_{TC} with or without FcεRI-and non-FcεRI stimulation were challenged with live HIV up to five days. As seen in Figure 1, MC_{TC} did not become infected with HIV under resting or any stimulated conditions as assessed by PCR of the HIV-specific marker p24. As a control CEM-GFP cells were actively infected as assessed by p24 expression and GFP upregulation (**Figure 1**) [5]. As expected no viral proteins were detected in the mast cell lysate using western blotting (not shown). This study suggests HIV does not infect human MC_{TC} or the progenitors that give rise to them and therefore do not serve as a reservoir for HIV [6].

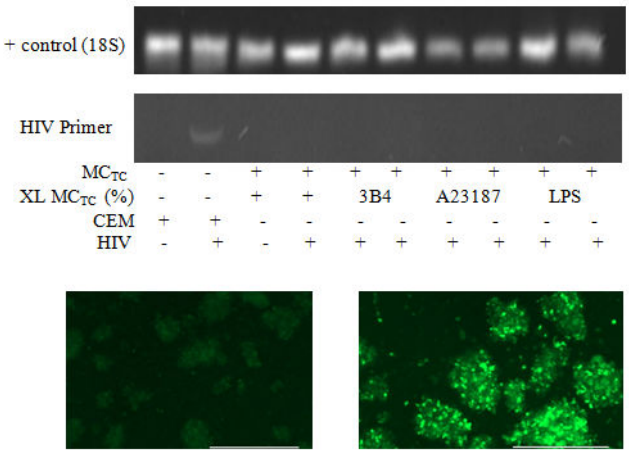

Figure 1: HIV does not infect human connective tissue mast cells.

MC_{TC} were plated in duplicate in a 24 well plate (5×10^5 cells/well) with (XL) or without various FcεRI-dependent (anti-FcεRI-alpha receptor antibody 3B4) or non-

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FcεRIdependent stimuli calcium ionophore (A23187, 0.1 µg/mL) or lipopolysaccharide (LPS; 1.5 µg/ml) overnight [7]. The average percent degranulation is given. The following day live HIV_{LAI} (NIH AIDS Reagent Program, Germantown, MD) was added to each well at a multiplicity of infection between 0.1 and 0.5 and incubated for 5 days. After 5 days cells were washed three times and left to incubate overnight in new, virus-free media to allow for any non-internalized virus to either infect or be released from non-specific adhesion to cellular plasma membranes [8]. After a final wash, cells were suspended in water for subsequent PCR preparation. For detection of viral DNA by PCR, the primers used were: Alu FWD: 5'-GCC TCA ATA AAG CTT GCC TTG A-3' and gag REV: 5'-CAT CTC TCT CCT TCT AGC CTC-3'.

CONCLUSION

DNA gels (A) shows HIV DNA amplicon (275bp) and 18s control primers (129bp). Experiments were repeated three times from normal donors. As a control virus was added to the CEM-GFP cell line (NIH AIDS Reagent Program, Germantown, MD) and viral uptake monitored by GFP. Representative CEM-GFP pictures above are: B: Uninfected; C: Infected. Scale bar represents 400 µm.

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