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LIVER NEUTROPHILS EXPRESS STRONGER PD-L1 SIGNALING IN HIV/HBV COMPARED TO HBV ALONE

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BACKGROUND

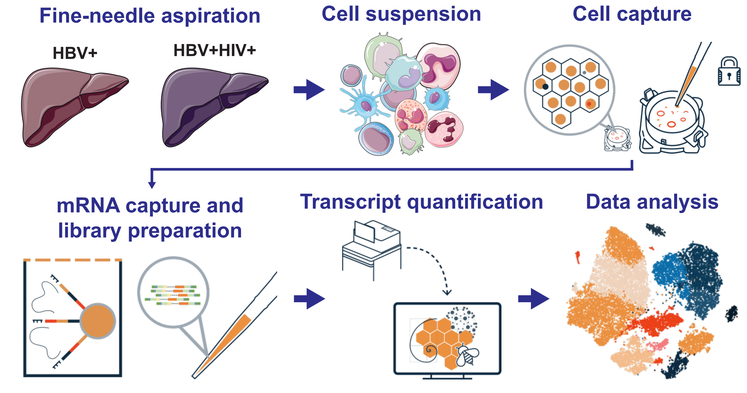
- High burden of HBV infection in Africa (~81 million with chronic HBV), and ~2.6 million people live with HIV/HBV coinfection.
- HIV coinfection accelerates the natural history of HBV infection; but precise mechanisms remain not fully understood.
- Understand how immune cells are modulated in the setting of HIV/HBV coinfection and suggest mechanisms for HBV functional cure in coinfection.

METHODS

- People living with HBV and HIV/HBV coinfection were recruited at the University Teaching Hospital (UTH, Lusaka, Zambia).
- Patients analyzed were treatment-naïve, no significant differences in demographics, liver enzymes, or HBV viral load were observed.

Patient Characteristics (n=12)		
Infection status	**HBV (n=6)**	**HIV/HBV (n=6)**
Age	32.5 (20-45)	33.83 (27-43)
Male Sex (%)	66.7%	66.7%
HBV viral load (IU/mL)	$2.39x10^8$ (6,400 -$7.95x10^8$)	$3.71x10^7$ (<10-$2.19x10^8$)
ALT (U/mL)	58.17 (27-145)	31.83 (17-61)
CD4 cell count (cells/mL)	N/A	309.67 (69-999)
HIV viral load (copies/mL)	N/A	$2.09x10^5$ (<60-$1.07x10^6$)

- Liver fine-needle aspirates (FNAs) were collected, loaded into HIVEs (*Honeycomb Biotechnologies*), and stored (-80°C) until shipment to Massachusetts General Hospital (MGH, Boston, USA.)
- Single-cell RNA sequencing (scRNA-seq) data were generated and analyzed at MGH.



- **Successful translation of liver FNA sampling for scRNA-seq to Africa**
- **Main immune cells were captured**
- **Analysis revealed a high ISG neutrophil subcluster that highly expressed PD-L1**

RESULTS

Figure 1: Overview of scRNA-seq dataset - Zambia cohort.

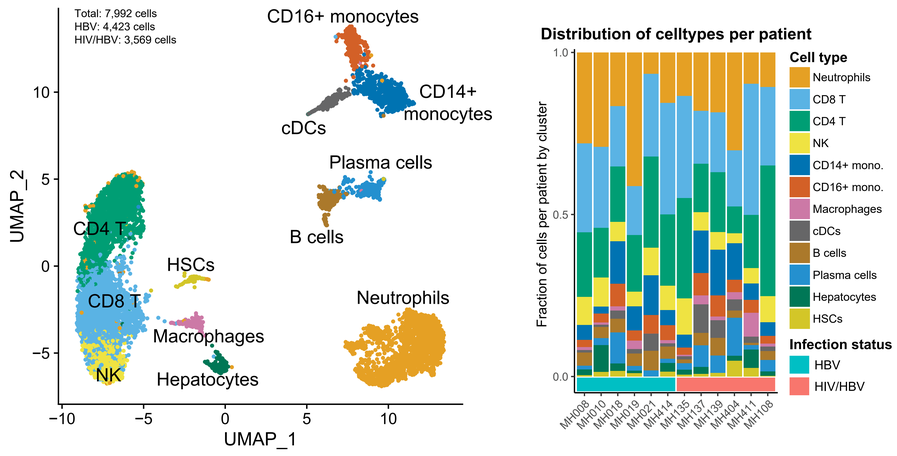


Figure 2: Differences in gene expression across immune cell types (A), and neutrophil pathway enrichment per disease status (B).

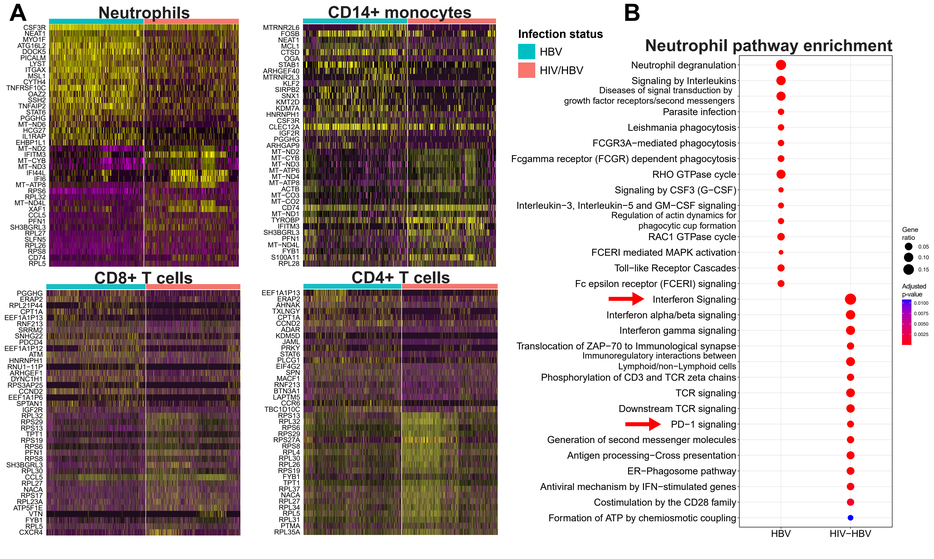


Figure 3: PD-1 and PD-L1/L2 expression (A), and CD8+ T cell pathway enirchment per disease status (B).

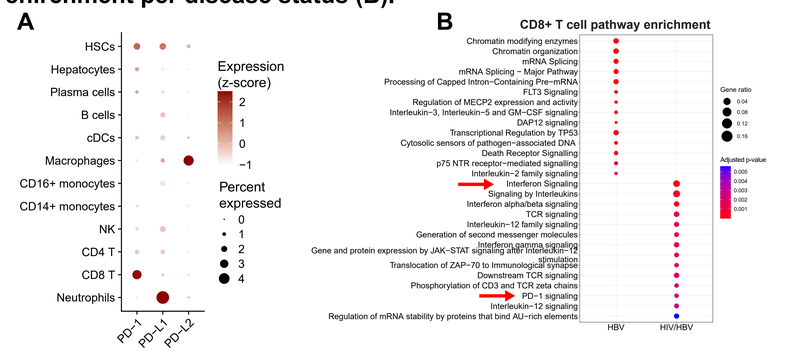
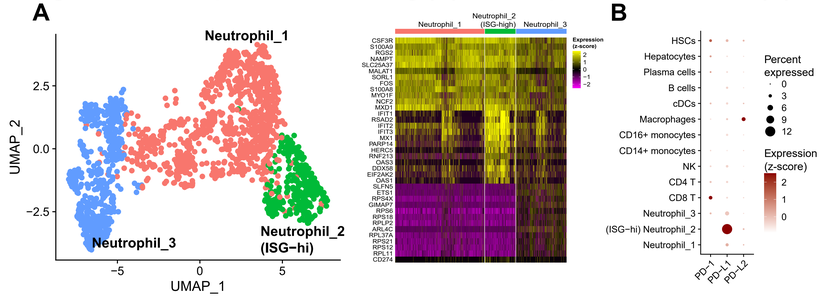


Figure 4: Neutrophil subclustering (A), and expression of PD-L1 (B).



CONCLUSIONS

- Expected myeloid/lymphoid immune populations as well as small numbers of macrophages, HSCs, and hepatocytes were captured in each patient (*Figure 1*).
- Neutrophils and CD8 T cells exhibited a stronger interferon and PD-1 signaling in HIV/HBV compared to HBV monoinfection (*Figures 2B & 3B*).
- Clustering of neutrophils revealed an ISG-high subcluster which strongly expressed PD-L1 (*Figure 4B*).

These data support neutrophil participation in the exhaustion and suppression of antiviral immune responses, a phenotype exacerbated in chronic HIV/HBV coinfection.

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