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P47

Poster for you

TIGIT-expression on NK cell subsets is an early indicator of alleviating liver inflammation following BLV treatment in chronic hepatitis D

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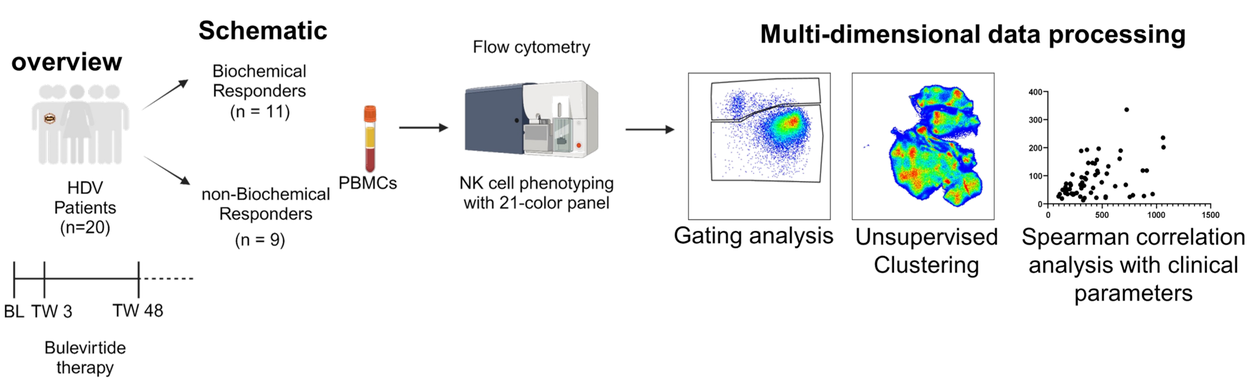
Introduction

With over 15 million cases worldwide, chronic Hepatitis D virus (HDV) infection (CHD) is a global health burden. CHD is the most severe form of chronic viral hepatitis that is associated with unfavorable outcomes, such as liver cirrhosis and hepatocellular carcinoma (HCC). Bulevirtide (BLV) was approved based on a phase 3 trial for the treatment of HDV. The study demonstrated a favorable risk-benefit ratio with significantly reduced HDV RNA and serum ALT levels in the patient. However, some patients are not responding by week 48 after therapy (TW48). Previous studies have shown that NK cells were functionally compromised in patients with CHD. Thus, the study aims to analyze NK cell immunotypes in patients with CHD during BLV therapy by using spectral flow cytometry and multi-dimensional data processing.

Study Design



Results

I Serum HDV RNA and ALT levels were significantly reduced while NK frequency remained stable

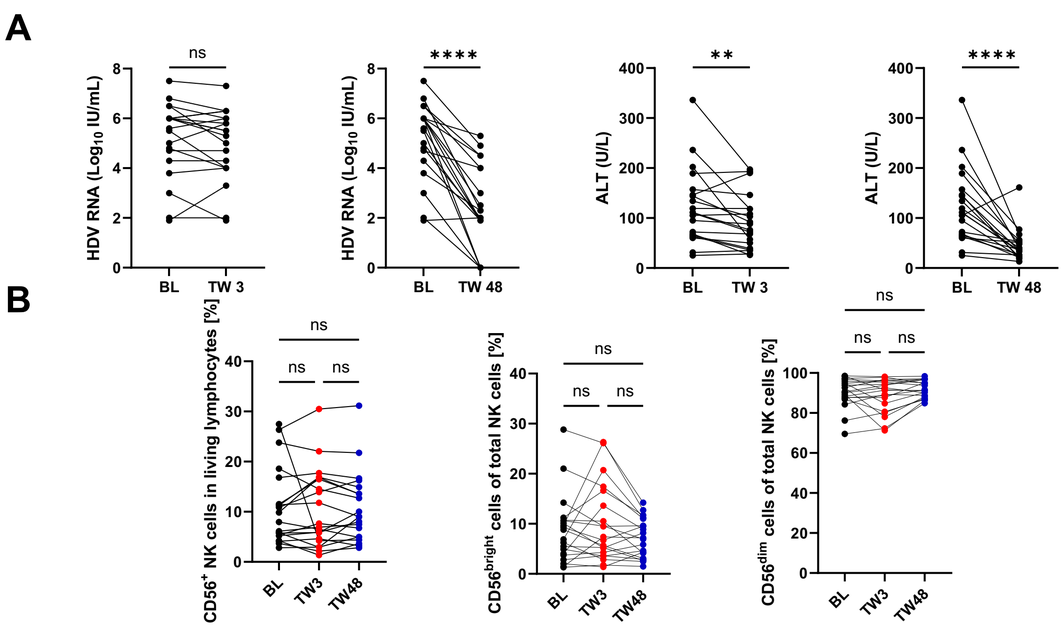
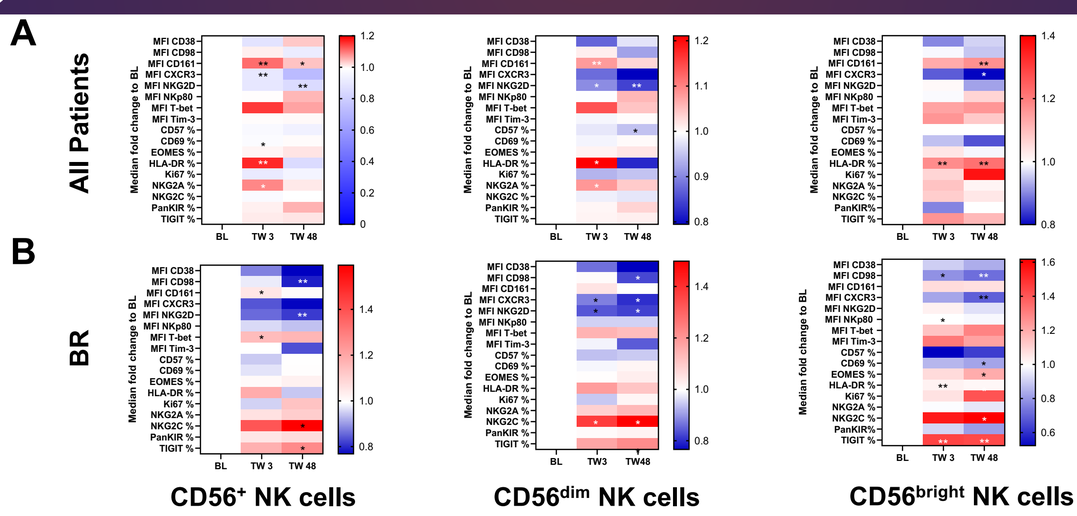


Fig 1. HDV RNA, ALT levels and NK frequency in HDV patients.

HDV patients received daily 2mg Bulevirtide, serum and PBMCs of patients were collected at BL, TW3 and TW48. **(A)** Pair-wise comparison of serum HDV RNA and ALT levels. **(B)** Qualification of frequency of $CD56^{+}$, $CD56^{dim}$ and $CD56^{bright}$ NK cells in HDV patients during Bulevirtide treatment.

II Longitudinal study revealed the most marked changes in Biochemical responder (BR)



$CD56^{+}$ NK cells **$CD56^{dim}$ NK cells** **$CD56^{bright}$ NK cells**

Fig 2. Longitudinal comparison of each marker expression on different NK cell subsets at all patients and BR group

(A) Heat maps of marker expression in all patients based on fold change of MFI or on percentage with longitudinal comparison referenced to BL. **(B)** Same analysis as in B for Biochemical Responder (BR).

III Unsupervised NK clustering revealed a therapy-sensitive NK clusters in BR

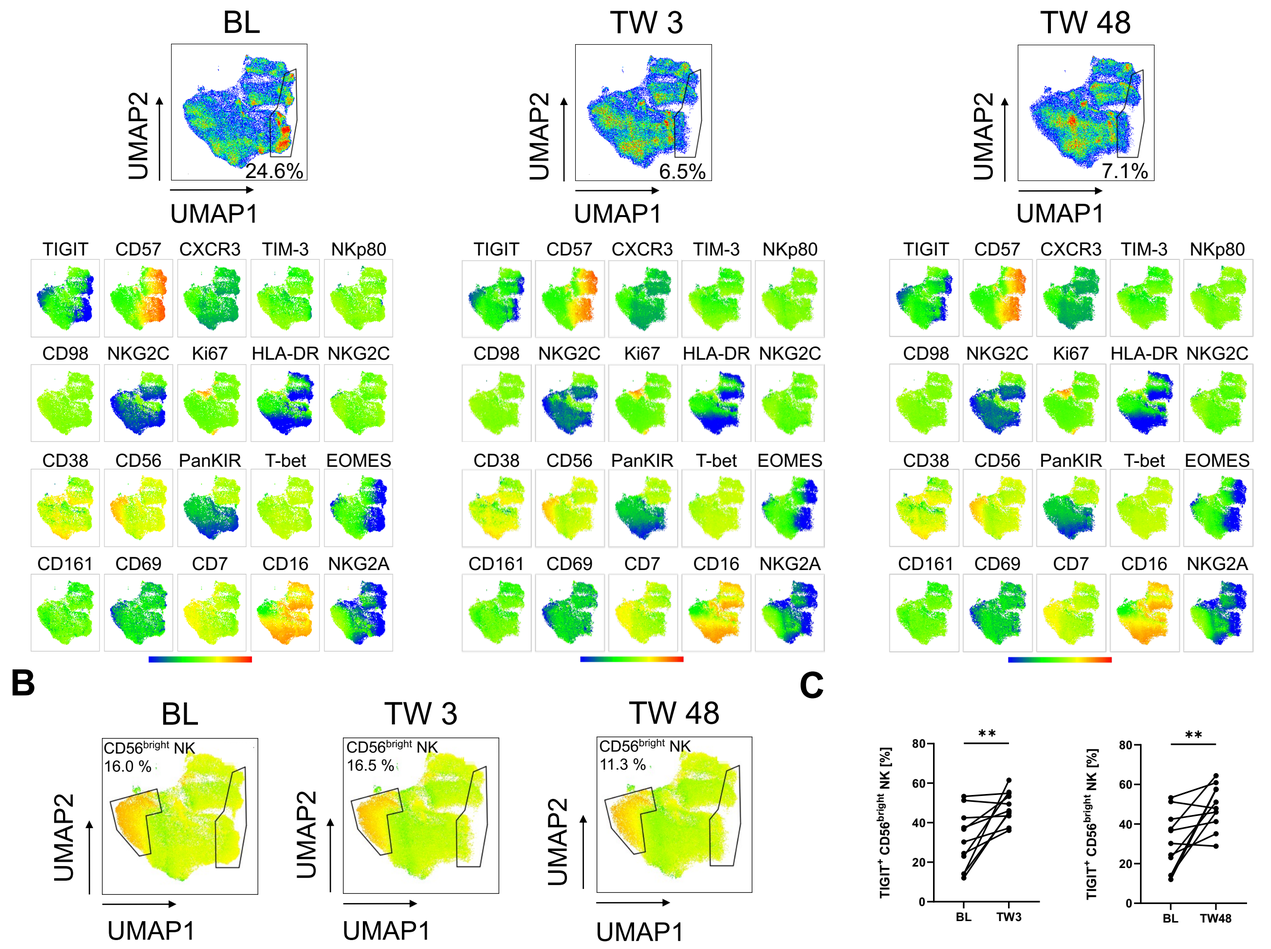


Fig 3. Identification and characterization of the therapy-sensitive NK cell immunotype

(A) Analysis of BR at BL, TW3 and TW48 including the UMAP plot and the multigraph color mapping. **(B)** UMAP showing the $CD56^{bright}$ NK cluster based on CD56 expression. **(C)** Upregulation of TIGIT expression on $CD56^{bright}$ NK cells at TW3 and TW48 compared to BL.

IV Expression of TIGIT-related NK subsets correlated with serum ALT but not viral load

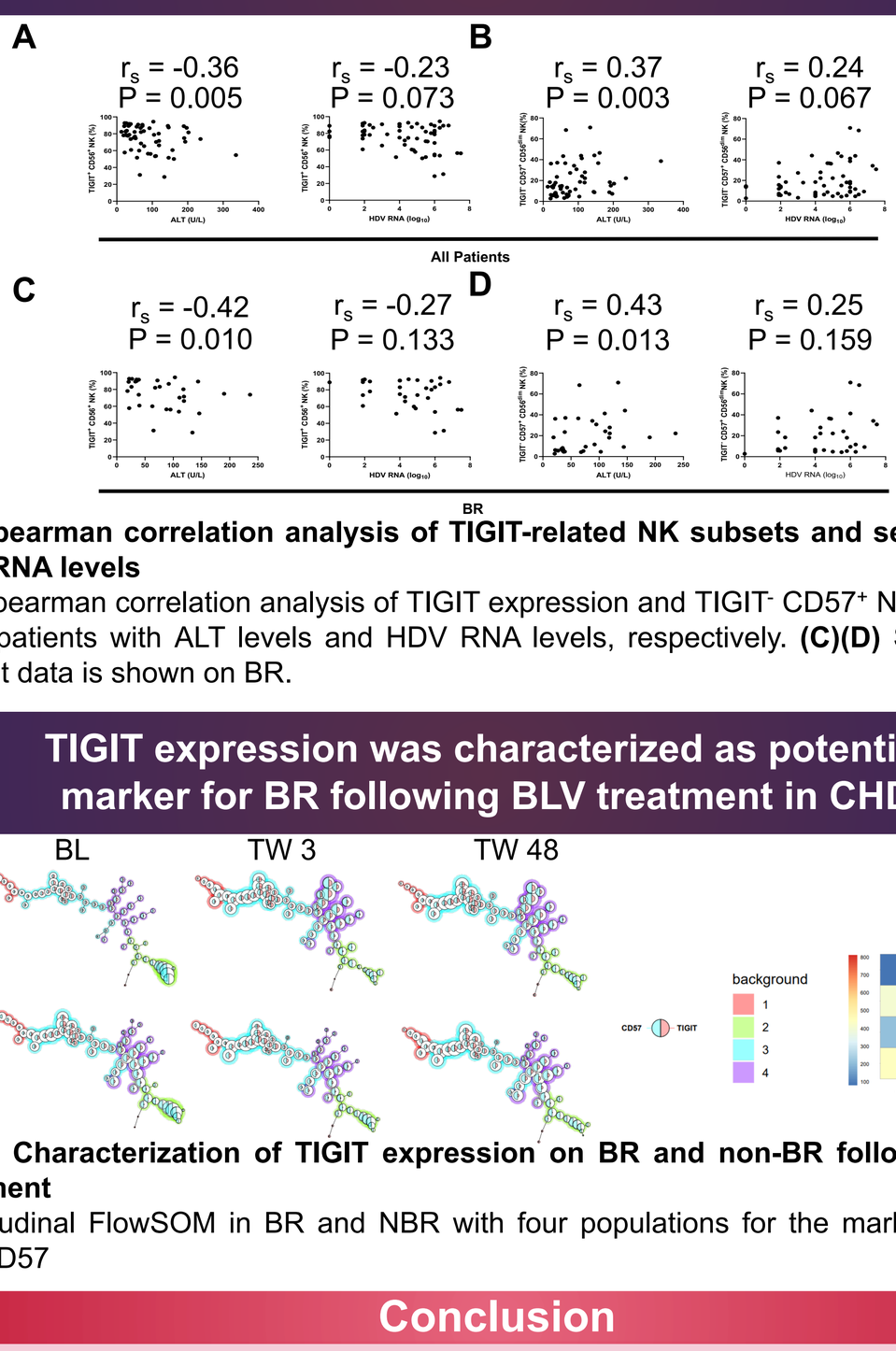


Fig 4. Spearman correlation analysis of TIGIT-related NK subsets and serum ALT or HDV RNA levels

(A)(B) Spearman correlation analysis of TIGIT expression and $TIGIT^{-}$ $CD57^{+}$ NK subsets from all patients with ALT levels and HDV RNA levels, respectively. **(C)(D)** Similar as (A)(B) but data is shown on BR.

V TIGIT expression was characterized as potential marker for BR following BLV treatment in CHD

Fig 5. Characterization of TIGIT expression on BR and non-BR following BLV treatment

Longitudinal FlowSOM in BR and NBR with four populations for the markers TIGIT and CD57

Conclusion

The absence of TIGIT expression on $CD57^{+}$ NK cells might be a hallmark of liver inflammation in HDV infection