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A real-world application of aqueous humor and vitreous fluid for the diagnosis of vitreoretinal lymphoma and treatment monitoring

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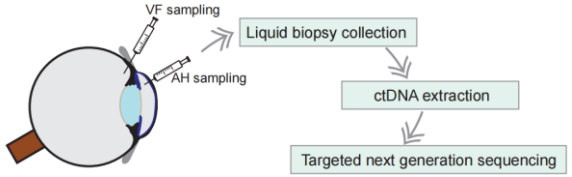
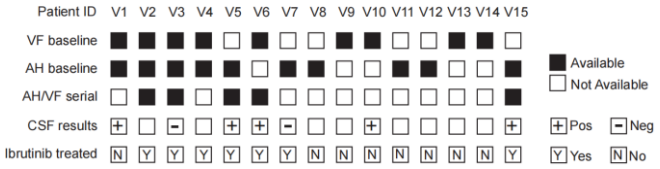
BACKGROUND

The diagnosis of vitreoretinal lymphoma (VRL), a rare subtype of primary central nervous system lymphoma (PCNSL), currently relies on the histopathology of vitreous biopsy. Misdiagnoses occasionally happen due to the extremely low number of cancerous cells in vitreous fluid (VF), and the examination of visual acuity and fundus can be subjective and inaccurate during VRL treatment monitoring. We aimed to investigate the mutational landscape of VRL and the application of the molecular profiling of AH ctDNA in treatment monitoring



METHODS

A total of 15 VRL patients whose baseline aqueous humor (AH) and/or vitreoretinal fluid (VF) specimen subject to comprehensive genomic profiling using targeted next generation sequencing. Sample availability is shown below.



FUTURE DIRECTIONS

1. The mutational features observed in this study need to be validated in larger cohort.
2. The response to ibrutinib-involved treatment in VRL is suboptimal and better therapeutics need to be investigated.

DISCLOSURE

The first author has no conflicts of interest to declare. This study was supported by the National Science & Technology Major Project (Grant number: 2017ZX09304021).

Aqueous humor (AH) represents a substitute for **vitreous fluid (VF)** as a **rich** source of **eye-specific** tumor genomic information

Highlights:

- Genetic alterations detected in AH ctDNA were **highly concordant** with those in paired VF ctDNA.
- NGS-based genomic profiling of AH ctDNA revealed a higher prevalence of ***IRF4*** mutation and ***CDKN2B*** deletion in VRL than in PCNSL, but a lower frequency of ***MYD88* L265P**.
- Molecular profiling of the AH ctDNA has great clinical utility for VRL **diagnosis and treatment monitoring**.

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RESULTS

Mutational comparison between matched AH, VF, and CSF samples

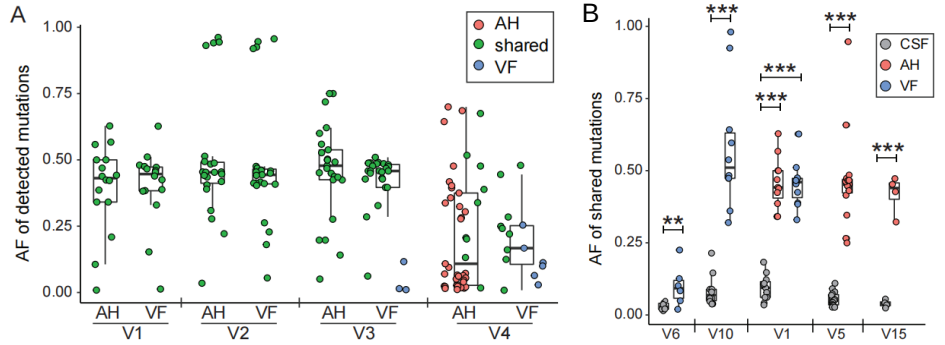

Fig. 1 (A) Four pairs of baseline AH and VF samples underwent targeted NGS. The allele frequencies (AF) of shared and unique mutations detected in matched AH and VF samples are shown. Two patients (V1 and V2) shared the identical mutational spectrum between AH and matched VF samples, and mutation allele frequencies (AFs) were comparable. (B) The AFs of shared mutations between CSF and AH/VF samples are presented here. **, p<0.05, ***, p<0.01. All five patients showed significantly higher AFs of shared mutations in AH and/or VF samples than CSF ctDNA.

Mutational feature comparison between VRL and PCNSL & *IRF4* mutation landscape in VRL

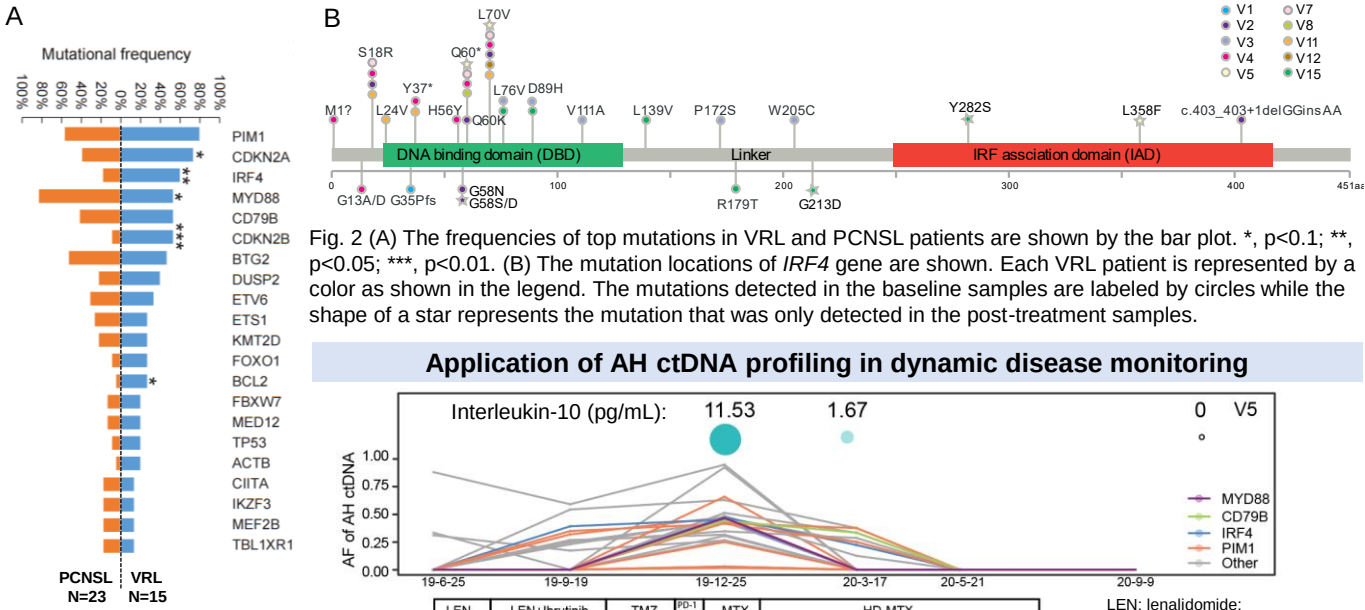

Fig. 2 (A) The frequencies of top mutations in VRL and PCNSL patients are shown by the bar plot. *, p<0.1; **, p<0.05; ***, p<0.01. (B) The mutation locations of *IRF4* gene are shown. Each VRL patient is represented by a color as shown in the legend. The mutations detected in the baseline samples are labeled by circles while the shape of a star represents the mutation that was only detected in the post-treatment samples.

Application of AH ctDNA profiling in dynamic disease monitoring

LEN: lenalidomide;
TMZ: temozolomide;
HD-MTX: high dose methotrexate