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Whole genome sequencing of Hepatitis Delta Virus (HDV) using next-generation sequencing: A new tool to detect nucleotide variations and phylogenotyping

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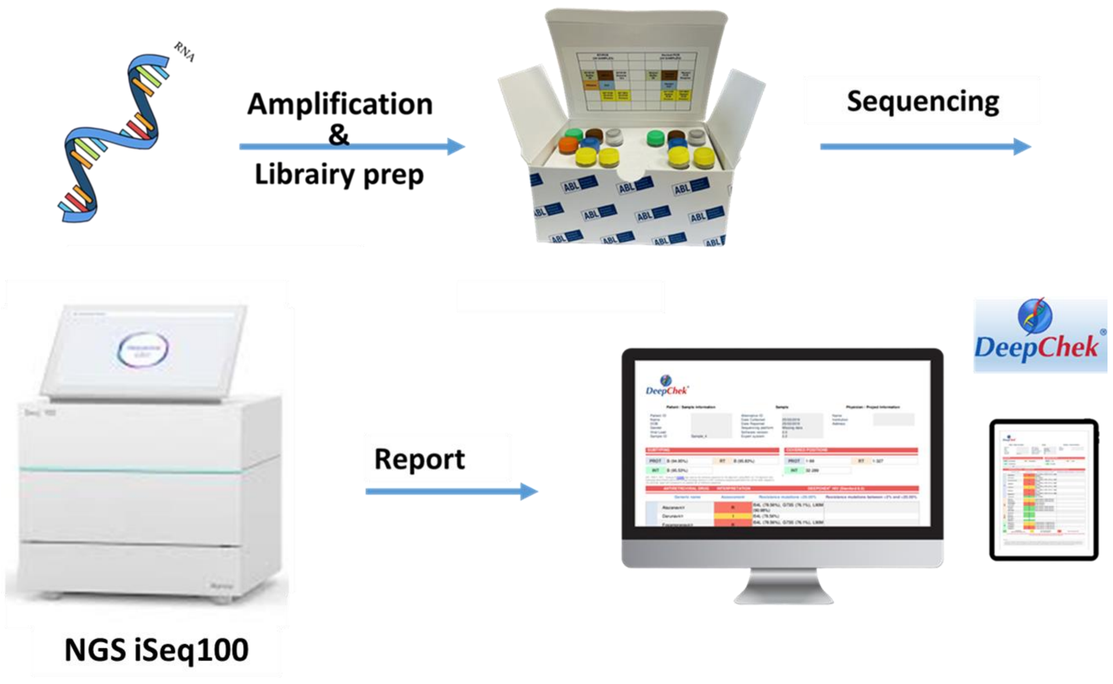
Introduction

Hepatitis Delta virus (HDV), a satellite of Hepatitis B virus (HBV), has a small circular RNA genome. HBV/HDV co-infections affect 15 to 20 million people worldwide and chronic hepatitis D is the most severe form of viral hepatitis among infected patients. It significantly increases the risk of cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Bulevirtide received conditional approval from the European Medicines Agency (EMA) in July 2020 pending FDA approval. The objective of this study was to evaluate the DeepChek® HDV (ABL) NGS sequencing assay, which can detect and list mutations.

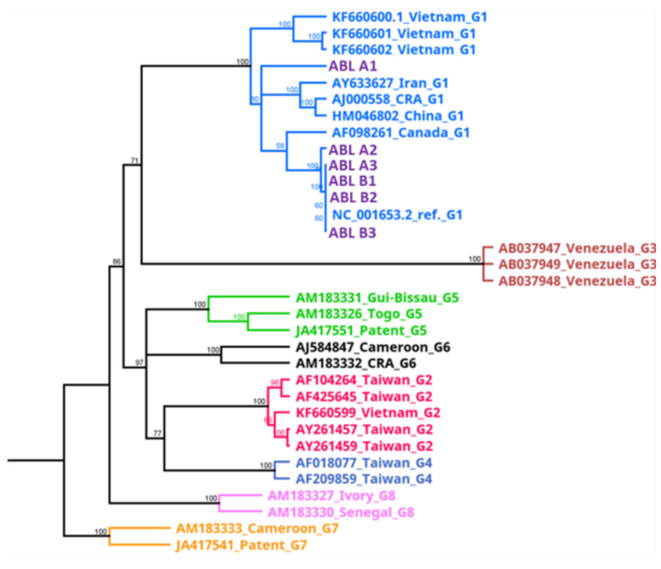
Methods

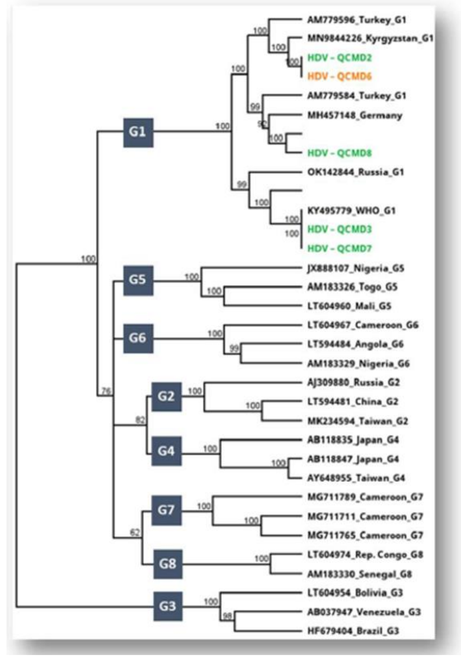
Eight positive human plasma samples, and 8 QCMD (Quality Control for Molecular Diagnostics) for HBV and HDV, were extracted with MagNa Pure 24 (Roche). HDV RNA amplification and library preparation were performed using the DeepChek® HDV (ABL) assay. NGS whole genome sequencing was performed using the iSeq100 (Illumina) model. The sequences were compared to the HDV reference genomes. The DeepChek® HDV Whole Genome (ABL) software was used to detect mutations and construct phylogenetic trees.



Results

Specimens were accurately genotyped. The mean coverage was 10,000 reads per sample and the Q30 was 87% (2x150 bps). HDV was detected in 6 of the 8 patients who tested positive for HBV. Phylogenotyping analysis was carried out to type the 12 sequences obtained (6 patients + 6 QCMD). They all belong to genotype 1, the most prevalent of the eight genotypes of HDV known to date.





Conclusions

The evaluation of the DeepChek® HDV (ABL) solution was conclusive. The construction of libraries combined with easy-to-use software made it possible to quickly and efficiently genotype the HDV virus present in the patients tested during this study. In the near future, NGS technology is set to play an increasingly important role in the genetic analysis of HIV, HCV and HBV/HDV viruses, thanks in part to lower costs and its ability to reveal variants or new mutations and study their impact.