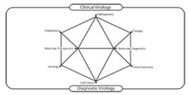
A Novel Software and Database Solution Tool for Analysis of Sanger and Next Generation Sequencing (NGS)



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Background

- Despite the potent antiviral activity of therapeutic options available for the treatment of chronic hepatitis B, HBV still persists.
- Long therapy is required and sometimes leads to the emergence of drug resistance. New insights into HBV drug resistance is stemming from the introduction of NGS, which identifies major and minor variants within the HBV RT.
- Specific algorithms managing Hepatitis B Surface Antigen (HBsAg) mutants as well are required for in-depth research, disease management and prevention.

Methods

- We used DeepChek-HBV, a software application in process of CE-IVD marking, to perform automated analysis of NGS and Sanger sequencing data.
- Antiviral resistance was assessed by DeepChek-HBV applying SeqHepB, Geno2pheno or Stanford algorithms and the EASL Clinical practical guidelines 2012 to the sequence data (*Fig 1*).

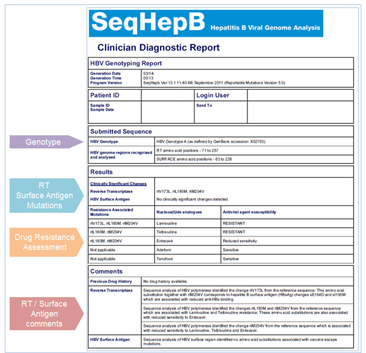

Fig. 2: Example of a SeqHepB report.

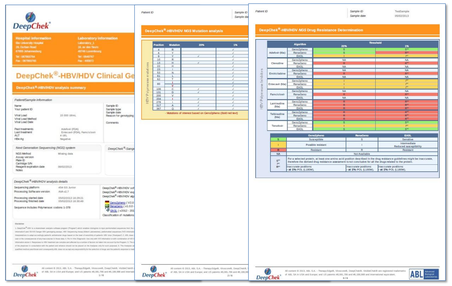

Fig. 1: Example of a DeepChek-HBV clinical genotyping report.

- Vaccine/immune escape and HBV genotype was determined through the analysis of the HBV surface gene by SeqHepB (*Fig. 2*).
- Through validation studies in Thailand, Turkey and the Netherlands, DeepChek-HBV permitted to harvest key HBV sequences coming from TruGene, ViroSeq, Roche-454 GS-Junior and Ion Torrent-PGM sequencers.

Results

- In a pool of 28 samples, DeepChek-HBV identified 8 (28.6%) and 10 (35.7%) samples harboring known drug resistance mutations at 20% and 1% thresholds, respectively (Fig. 3).
- Mutations causing reduction in drug susceptibility were observed in 6, 7, 7, 7, 0 samples for Adefovir, Entecavir, Lamivudine, Telbivudine and Tenofovir respectively (*Fig. 4*).

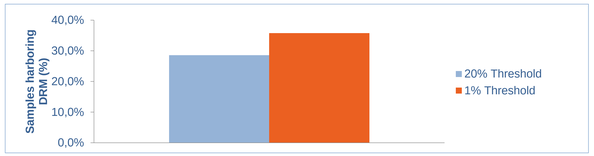

Fig. 3: Percentage of samples harboring at least one DRM at 20% (blue) and 1% (red) thresholds.

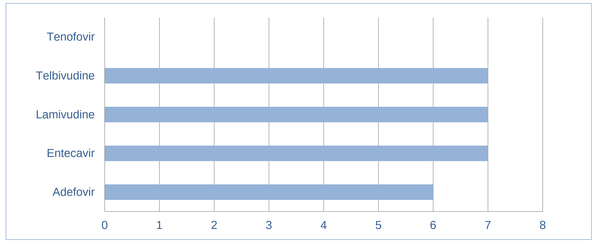

Fig. 4: Overview of the number of samples where an increase of the drug resistance has been observed per drug using the Geno2Pheno algorithm comparing interpretations given at 20 and 1%.

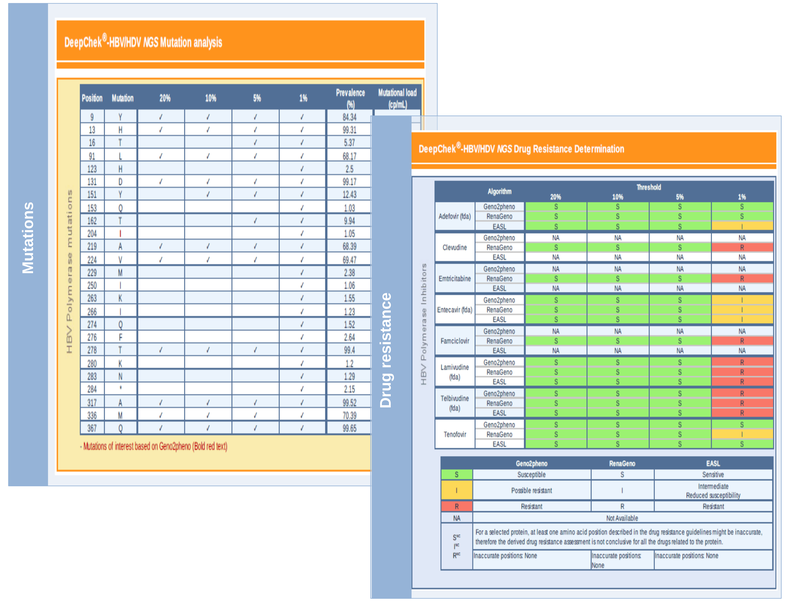

Fig. 5: DeepChek®-HBV reporting of HBV RT mutations and drug resistance interpretations for 1 sample harboring minor drug resistance mutation (204I).

Conclusions

- This study illustrated the benefits of combining well-validated downstream analysis software and updated knowledge database for managing HBV Sanger and NGS outputs.
- Such solution can be extended nationwide as an innovative service for the management of CHB and establishment of national HBV databases for personalized medicine.

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1117