DRUG-RESISTANT MUTATION 1

```
      10----------------------------20----------------------------
            -|-------------------------------|----------------------------
Input       _-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-_
Consensus   _G__E__H__H__I__R__I__P__R__T__P__A__R__V__T__G__G__V__F__L_
Consensus   ggagaacatcacatcaggattcctaggacccctgctcgtgttacaggcggggtttttctt
Input       ....c.a.a.t.....c....t..c....ag.....t...ca...t.....acg--....
            --|---------|---------|---------|---------|---------|-------
            -30--------40--------50--------60--------70--------80-------

            30----------------------------40----------------------------
            -|-------------------------------|----------------------------
Input       _-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-_
Consensus   _V__D__K__N__P__H__N__T__A__E__S__R__L__V__V__D__F__S__Q__F_
Consensus   gttgacaagaatcctcacaataccgcagagtctagactcgtggtggacttctctcaattt
Input       ...t..gtccg...g.tg...c....g..----c...-.c--c.---.g-.g...g----
            --|---------|---------|---------|---------|---------|-------
            -90--------100-------110-------120-------130-------140------

            50----------------------------60----------------------------
            -|-------------------------------|----------------------------
Input       _-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-__-_
Consensus   _S__R__G__N__Y__R__V__S__W__P__K__F__A__V__P__N__L__Q__S__L_
Consensus   tctagggggaactaccgtgtgtcttggccaaaattcgcagtccccaacctccaatcactc
Input       -..t--....t...-------..g.---.c-cc...t.c.....gt......g.c...g.
            --|---------|---------|---------|---------|---------|-------
            -150-------160-------170-------180-------190-------200------

            70----------------------------80----------------------------
            -|-------------------------------|----------------------------
Input       _X__X__.__X__X__.__Q__P__V__.__I__Y__I__S__M__A__.__R__V__._
Consensus   _T__N__L__L__S__S__N__L__S__W__L__S__L__D__V__S__A__A__F__Y_
Consensus   accaacctcctgtcctccaacttgtcctggttatcgctggatgtgtctgcggcgttttat
Input       -g.-.--------...----.----t..--...-...-...--c.....t-..c--..c.
            --|---------|---------|---------|---------|---------|-------
            -210-------220-------230-------240-------250-------260------

           90----------------------------100----------------------------
            -|-------------------------------|----------------------------
Input       _Q__.__D__S__R__D__V__L__R__.__-__-__-__.__.__A__E__S__R__G_
Consensus   _H__L__P__L__H__P__A__A__M__P__H__L__L__V__G__S__S__G__L__S_
Consensus   catcttcctcttcatcctgctgctatgcctcatcttcttgttggttcttctggactatca
Input       .........g.g..--..t.-...tca....tg.-a....c...ac.acg..a..c...-
            --|---------|---------|---------|---------|---------|-------
            -270-------280-------290-------300-------310-------320------

            110----------------------------120----------------------------
            -|-------------------------------|----------------------------
Input       _.__P__L__.__.__.__.__.__P__.__S__A__V__P__S__D__.__.__A__-_
Consensus   _R__Y__V__A__R__L__S__S__N__S__R__I__F__N__H__Q__H__G__T__M_
Consensus   aggtatgttgcccgtttgtcctctaattccaggatcttcaaccaccagcacgggaccatg
Input       .--g..cc.....aag-..-..-....aag........gg..tc......t.ta..g.c-
            --|---------|---------|---------|---------|---------|-------
            -330-------340-------350-------360-------370-------380------

            130----------------------------140----------------------------
            -|-------------------------------|----------------------------
Input       _-__-__-__.__L__.__L__-__-__R__-__-__-__G__.__P__V__C__-__-_
Consensus   _Q__N__L__H__D__S__C__S__R__N__L__Y__V__S__L__L__L__L__Y__Q_
Consensus   cagaacctgcacgactcctgctcaaggaacctctatgtatccctcctgttgctgtaccaa
Input       .---....tg.g.c..a..--....a.-.-..g.g...t.aaaga......a....--..
            --|---------|---------|---------|---------|---------|-------
            -390-------400-------410-------420-------430-------440------

            150----------------------------160----------------------------
            -|-------------------------------|----------------------------
Input       _A__.__S__S__A__G__-__-__-__-__-__.__C__A__.__R__.__E__T__V_
```

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Consensus   _T__F__G__R__K__L__H__L__Y__S__H__P__I__I__L__G__F__R__K__I_
Consensus   accttcggacggaaattgcacctgtattcccatcccatcatcctgggctttcggaaaatt
Input       .--..a...a........-----..c.g.g..--........a..caac..-------..
            --|---------|---------|---------|---------|---------|-------
            -450-------460-------470-------480-------490-------500------

            170---------------------------180---------------------------
            -|-----------------------------|----------------------------
Input       _A__H__Q__I__-__.__-__.__K__V__.__H__K__R__.__L__G__L__P__._
Consensus   _P__M__G__V__G__L__S__P__F__L__L__A__Q__F__T__S__A__I__C__S_
Consensus   cctatgggagtgggcctcagcccgtttctcctggctcagtttactagtgccatttgttca
Input       t.-----------a....t.-..--.aa..a.ct..t-.--...at..c.....c.c...
            --|---------|---------|---------|---------|---------|-------
            -510-------520-------530-------540-------550-------560------

            190---------------------------200---------------------------
            -|-----------------------------|----------------------------
Input       _T__T__D__L__.__.__K__D__.__V__D__W__E__E__L__G__E__E__I__V_
Consensus   _V__V__R__R__A__F__P__H__C__L__A__F__S__Y__M__D__D__V__V__L_
Consensus   gtggttcgtagggctttcccccactgtttggctttcagttatatggatgatgtggtattg
Input       c.-.---.-g........t..t.t.....---..c.c..gg.ca....c.--.--.c...
            --|---------|---------|---------|---------|---------|-------
            -570-------580-------590-------600-------610-------620------

            210---------------------------220---------------------------
            -|-----------------------------|----------------------------
Input       _.__I__N__.__A__H__.__H__H__A__T__.__S__P__L__P__.__-__-__-_
Consensus   _G__A__K__S__V__Q__H__L__E__S__L__F__T__A__V__T__N__F__L__L_
Consensus   ggggccaagtctgtacagcatcttgagtccctttttaccgctgttaccaattttcttttg
Input       .at.---.--....t.t.-----.---..t..c.c.--.a.----..a....ac..gc..
            --|---------|---------|---------|---------|---------|-------
            -630-------640-------650-------660-------670-------680------

            230---------------------------240---------------------------
            -|-----------------------------|----------------------------
Input       _-__-__-__-__.__.__L__-__-__-__-__-__-__-__-__.__M__S__.__._
Consensus   _S__L__G__I__H__L__N__P__N__K__T__K__R__W__G__Y__S__L__H__F_
Consensus   tctttgggtatacatttaaaccctaacaaaacaaaaagatggggttactctttacatttc
Input       c.gg....gggg-----.g.----..a....a...nn-----------------------
            --|---------|---------|---------|---------|---------|-------
            -690-------700-------710-------720-------730-------740------

                                250---------------
                                -|----------------
                     Input       _S__S__L__N__L__.
                     Consensus   _M__G__Y__V__I__G
                     Consensus   atgggctatgtcattgg
                     Input       -----------------
                                 --|---------|----
                                 -750-------760---
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Sequence Alignment

Alignment between the input query sequence and the genotype D consensus reference sequence. Amino acid and nucleotide sequence numbers refer to HBV polymerase numbering.

Figure S1. Drug-resistant mutation observed in a case of HBV-related HCC from South India. The input sequence (yellow) bears an amino acid I in place of the expected L, as observed in the reference sequence (green) at codon 80 (blue). The mutation L80I is a lamivudine mutation and a compensatory mutation for M204V/I.