

## Supplementary Materials:

**Supplementary Table S1.** Primers used in the study.

| Amplicon                            | Forward primer (5'-3')*                                                 | Reverse primer (5'-3') <sup>1</sup>                                                      |
|-------------------------------------|-------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Genome cloning<br>(fragment 1)      | <u>GATATACATATGGCTAGCTAATACGA</u><br><u>CTCACTATAGCAGACCACGTATGTGGT</u> | <u>TGGCCCTTTCGTCTTCAAGAATTAATT</u><br><u>CCGCCTTCTTAAGAAATGTCCTACAAC</u>                 |
| Genome cloning<br>(fragment 2)      | <u>GCCGTGTAGGACATTTCTTAAGA</u><br><u>AGGCTGTGGGTAAGTTCTGCTGTT</u>       | <u>TGGCCCTTTCGTCTTCAAGAATTAA</u><br><u>ATTCCAGCAGCATCGATCTCCAGT</u>                      |
| Genome cloning<br>(fragment 3)      | <u>CCAACCTAGCACTGGAGATCGATGC</u><br><u>TGCTACGGAGGTCGGCCGGGCTTG</u>     | <u>TGGCCCTTTCGTCTTCAAGAATTAA</u><br><u>TTCCTACACACTCGAGACCAAGGG</u>                      |
| Genome cloning<br>(fragment 4)      | <u>CCCTTGGTCTCGAGTGTGTAGTCAT</u><br><u>GGAGGAATGTGGCATGCCCCAGTG</u>     | <u>CGTCTTCAAGAATTAATTCCATTTCG</u><br><u>TACCGGTGAAGTGCAGGTCCTTCA</u>                     |
| Genome cloning<br>(fragment 5)      | <u>ATGAAGGACCTGGACTTCACCGGTAC</u><br><u>GAATGGGGTCGGTGAGGTGGGTCGT</u>   | <u>CTGGCCCTTTCGTCTTCAAGAATTA</u><br><u>ATTCCGCGCACGCGTTTTTTTTTTT</u>                     |
| Determination<br>of 3' end (pair A) | ACTTTTGATGATTTCTGCCCCG                                                  | GGAGCGCGAAACGCAGA                                                                        |
| Determination<br>of 3' end (pair B) | ACTTTTGATGATTTCTGCCCCG                                                  | CCGAATTCCCGGGATCCTTTTTTTTTT<br>TTTTTV (reverse transcription)<br>CCGAATTCCCGGGATCC (PCR) |
| Determination<br>of 3' end (pair C) | ACTTTTGATGATTTCTGCCCCG                                                  | ATGTGAGTTAGCTCACTCATTAGGC                                                                |
| Analysis of<br><i>Eco</i> RI site   | TGTACACCCGGACATGGTCA                                                    | CCCTACATACACCTTTGCCCC                                                                    |

<sup>1</sup>Nucleotides binding to the parental plasmid in the second PCR reaction are underlined.

**Supplementary Table 2:** Nucleotide exchanges identified between the initial genomic clone, HEV in patient serum, HEV after cell culture isolation (low passage) and the final genomic plasmid p47832mc.

| Nucleotide position | Patient serum | Low-passaged cell culture virus | Genomic clone | Amino acids   | Corrected genomic plasmid <sup>1</sup> |
|---------------------|---------------|---------------------------------|---------------|---------------|----------------------------------------|
| 37                  | C             | C                               | T             | Silent        | T                                      |
| 589                 | T             | C                               | T             | Silent        | T                                      |
| 1081                | T             | T                               | C             | Silent        | C                                      |
| 2072                | T             | T                               | C             | S683P (ORF1)  | T                                      |
| 2144                | A             | A                               | G             | T707A (ORF1)  | A                                      |
| 2409                | T             | T                               | C             | V795A (ORF1)  | T                                      |
| 2833                | C             | C                               | A             | Silent (ORF1) | C                                      |
| 2850                | C             | C                               | T             | A942V (ORF1)  | C                                      |
| 2926                | C             | C                               | T             | Silent (ORF1) | C                                      |
| 2966                | G             | G                               | A             | G981E (ORF1)  | G                                      |
| 3234                | G             | G                               | A             | R1070Q (ORF1) | G                                      |
| 3372                | A             | A                               | G             | Q1116R (ORF1) | A                                      |
| 4261                | C             | C                               | T             | Silent (ORF1) | T                                      |
| 4918                | C             | T                               | C             | Silent (ORF1) | C                                      |
| 5574                | G             | A                               | G             | R73G (ORF2)   | A                                      |
|                     |               |                                 |               | Silent (ORF3) |                                        |
| 5637                | C             | C                               | T             | P94S (ORF2)   | C                                      |
|                     |               |                                 |               | Silent (ORF3) |                                        |
| 5855                | T             | T                               | C             | Silent (ORF2) | C                                      |
| 6176                | T             | C                               | T             | Silent (ORF2) | T                                      |
| 6263                | C             | C                               | T             | Silent (ORF2) | C                                      |
| 6337                | C             | C                               | T             | A327V (ORF2)  | C                                      |
| 6417                | C             | C                               | G             | H354D (ORF2)  | C                                      |
| 6960                | A             | A                               | G             | T535A (ORF2)  | A                                      |
| 7065                | C             | T                               | C             | Silent (ORF2) | C                                      |
| 7315                | A             | A                               | G             | K653R (ORF2)  | A                                      |

<sup>1</sup>Exchanged nucleotides in p47832mc are indicated in bold face.