

Supplementary Table 1: List of the primers used to amplify the *macro domain* of Hepatitis E virus (HepMD). The 5' PCR halves are amplified using the HepMD_XXFW/HepMD_int_RV couples of primers. The 3' PCR halves are amplified using the HepMD_XXRV/HepMD_int_FW couples of primers. The PCR 2 is performed with primers PCR2_FW and PCR2_RV. This second PCR is based on hybridization between i) 5' and 3' PCR halves thanks to the overlapping sequences between HepMD_int_RV and HepMD_int_FW ii) HepMD_XXFW and PCR2_FW (the overlapping sequence corresponds to the coding sequence of the TEV protease cleavage site, as described previously , and iii) HepMD_XXRV and PCR2_RV. The overlapping sequences are represented in underlined italic. The melting temperature of the overlapping sequences is 60°C +/- 4°C to enable a good annealing of the primers.

Step	Primer Name	Primer sequence
5' PCR halves	HepMD_38FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> GCAACAGCACGTGCACCGGCAATTAC 3'
	HepMD_43FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> CCGGCAATTACCCATCAGGCAGCAC 3'
	HepMD_47FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> CATCAGGCAGCACGTACATCGTC 3'
	HepMD_52FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> CATCGTCCTGCTGTTACCTATCCG 3'
	HepMD_55FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> CTGCTGTTACCTATCCGGATGGTAGC 3'
	HepMD_60FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> CCGGATGGTAGCAAAGTTTGAGGC 3'
	HepMD_64FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> AAAGTTTGAGGCAGCCTGTTGAAGCAC 3'
	HepMD_76FW	5' <u>GAAAACCTGTACTTCCAGGGT</u> ACCTGGCTGGTTAATGCAAGCAATGTTGATC 3'
	HepMD_int_RV	5' <u>AATAATCGGACGCCGTGTCAGGGT</u> TATATGCAG 3'
3' PCR halves	HepMD_201RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAAACGATTGCTCAAACCAACGAGCAGCC 3'
	HepMD_205RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTACGGACAGGTGCGACGATTGCTCAAAC 3'
	HepMD_208RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAGGTCAAGGGTCGGACAGGTGCG 3'
	HepMD_214RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTATGCAACATCTCGGTAATGGTCAGGGTC 3'
	HepMD_218RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAAATTGCGGTACGTGCAACATCTCGGTAATG 3'
	HepMD_224RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAAATCCAGTTCAATGCCAGATTGCGGTAC 3'
	HepMD_230RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAAACCAACATCGGTTGCGCTATCCAGTTC 3'
	HepMD_235RV	5' <u>ACCACTTTGTACAAGAAAGCTGGGTCTT</u> ATTAAACCTGCACATGCACGACCAACATCGG 3'
	HepMD_int_FW	5' <u>CTGACACCGCGTCCGATTATT</u> CATGCAGTT 3'
PCR2	PCR2_FW	5' GGGGACAAGTTGTACAAAAAAGCAGGCTTA <u>GAAAACCTGTACTTCCAGGGT</u> 3'
	PCR2_RV	5' GGGG <u>ACCACTTTGTACAAGAAAGCTGGGT</u> C 3'