

1 **TABLE S1. Estimation of mating efficiency between bait and prey strains.**

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Viral bait	Cell density of bait culture	Cell density of prey culture	No. of cfu/ml on T	No. of cfu/ml on L	No. of cfu/ml on LT	% Mating efficiency	No. of diploid clones screened (million)
a. Estimation of mating efficiency between Y2H gold (g-1 HEV proteins) and Y187 (human fetal brain cDNA library)							
Met	1.4*10 ⁸	6.1*10 ⁷	8.4*10 ⁷	1.3*10 ⁶	1.8*10 ⁴	1.3	0.20
Y	1.2*10 ⁸	6*10 ⁷	8.4*10 ⁷	2*10 ⁶	8.4*10 ⁴	1.7	0.39
PCP	1.1*10 ⁸	3.8*10 ⁷	2.6*10 ⁷	2*10 ⁶	1.7*10 ⁵	8.85	2.03
V	1.5*10 ⁸	3.2*10 ⁷	5.8*10 ⁷	1.3*10 ⁶	1*10 ⁵	7.2	1.1
X	1*10 ⁸	4*10 ⁷	4*10 ⁸	8*10 ⁷	5.3*10 ⁵	0.6	6
Helicase	1.1*10 ⁸	3*10 ⁷	9.5*10 ⁷	1.5*10 ⁶	4.5*10 ⁴	2.9	0.51
RdRp	1.1*10 ⁸	3.5*10 ⁷	9.4*10 ⁷	1.8*10 ⁶	4.3*10 ⁴	2.3	0.5
ORF2	1.3*10 ⁸	3*10 ⁷	7.2*10 ⁷	2.5*10 ⁶	3.8*10 ⁴	2.7	2.4
ORF3	1*10 ⁸	2*10 ⁷	1.8*10 ⁸	1.6*10 ⁶	8.5*10 ⁴	5.3	.96
ORF4	1.1*10 ⁸	3.2*10 ⁷	9.1*10 ⁷	1.65*10 ⁷	2.1*10 ⁴	1.2	0.24

b. Estimation of mating efficiency between Y2H gold (g-1 HEV proteins) and Y187 (human liver cDNA library)

Met	1.1*10 ⁸	1*10 ⁸	1.4*10 ⁸	2.7*10 ⁶	1.3*10 ⁶	5.03	1.5
Y	1*10 ⁸	9*10 ⁷	4.6*10 ⁷	7*10 ⁶	2.7*10 ⁵	3.8	3.1
PCP	1.1*10 ⁸	3.4*10 ⁷	4.7*10 ⁷	2.8*10 ⁶	4.6*10 ⁵	1.6	5.29
V	1*10 ⁸	1*10 ⁸	3.1*10 ⁷	1.5*10 ⁶	2.3*10 ⁵	15.3	2.6
X	1.1*10 ⁸	7.5*10 ⁷	4.3*10 ⁷	3.1*10 ⁶	3*10 ⁵	9.8	3.5
Hel	1.1*10 ⁸	1*10 ⁸	1.3*10 ⁸	3.2*10 ⁶	8.9*10 ⁵	2.7	1.02
RdRp	1*10 ⁸	6.5*10 ⁷	3.7*10 ⁷	3.7*10 ⁶	1.4*10 ⁵	4	1.7
ORF2	1.4*10 ⁸	4*10 ⁷	8.5*10 ⁷	7.2*10 ⁶	2*10 ⁵	1.52	4.3
ORF4	1*10 ⁸	3*10 ⁷	9.64*10 ⁷	1*10 ⁶	2.8*10 ⁴	2.5	0.32

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4 L: Leucine, T: Tryptophan, “-”: Deficiency in the medium, “+”: Supplemented in the

5 medium, cfu: colony forming unit.

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