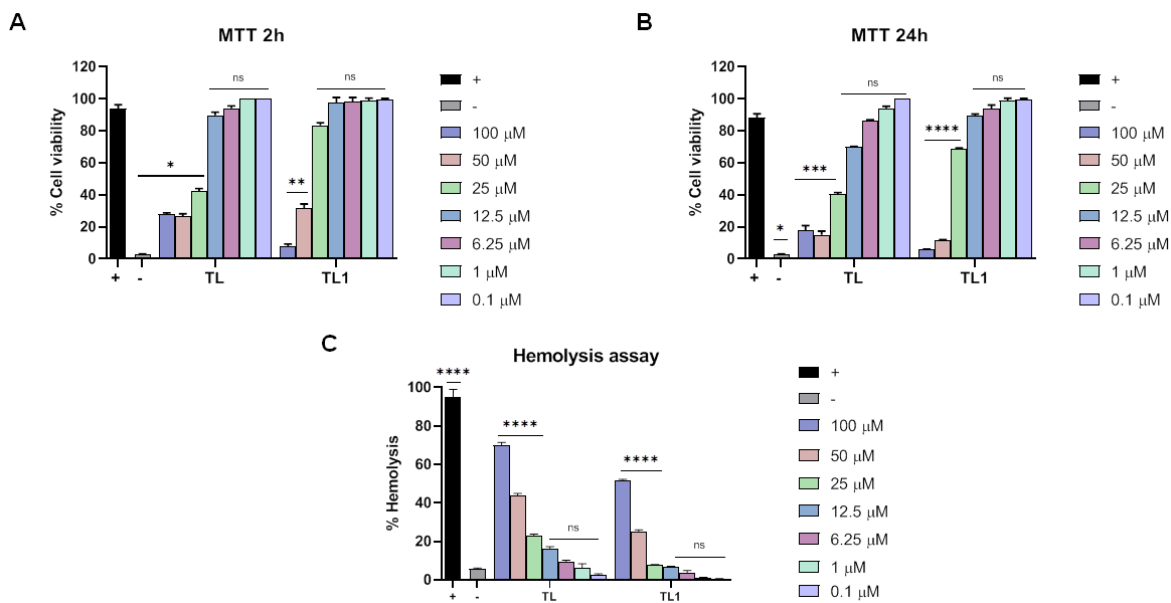
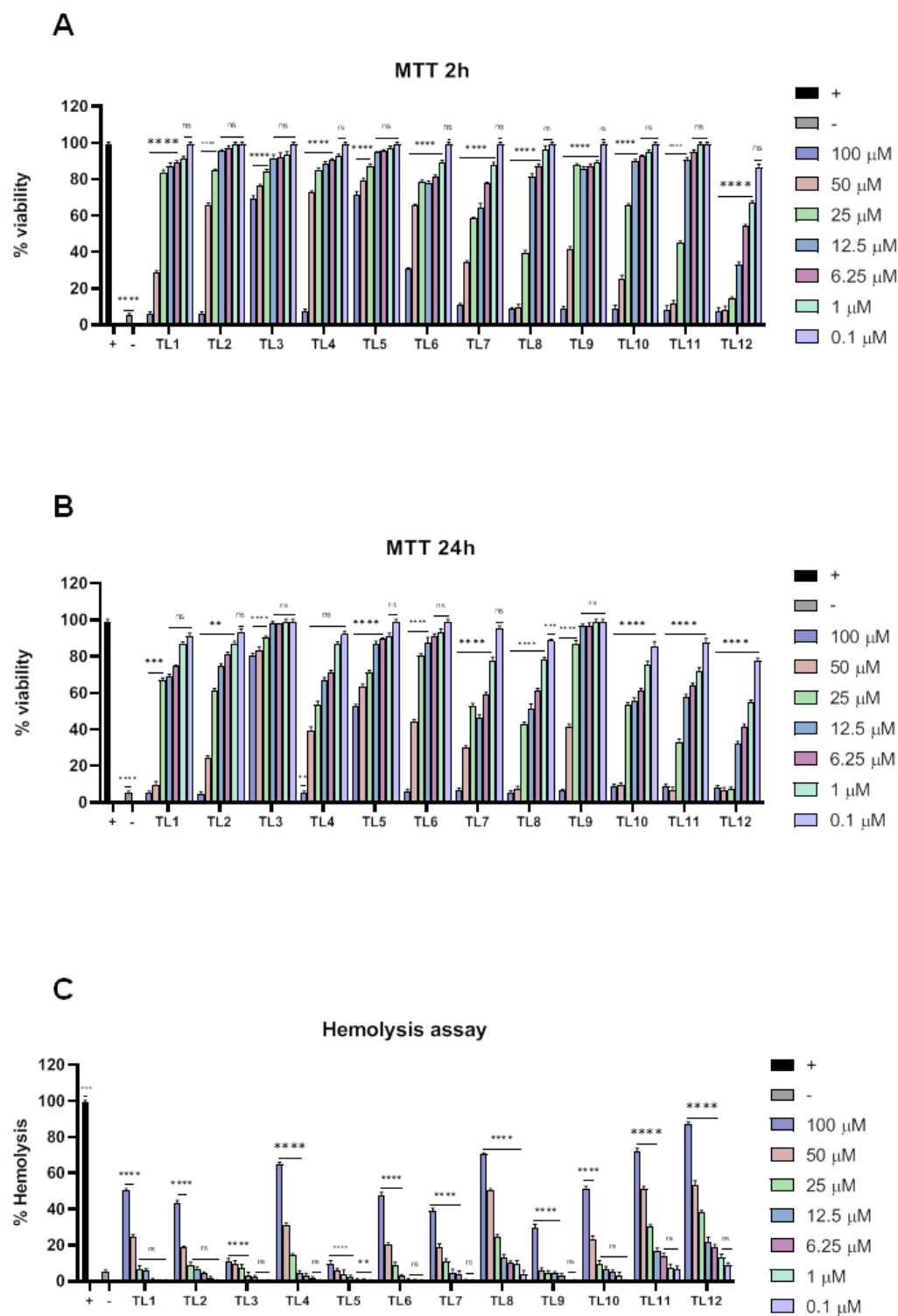


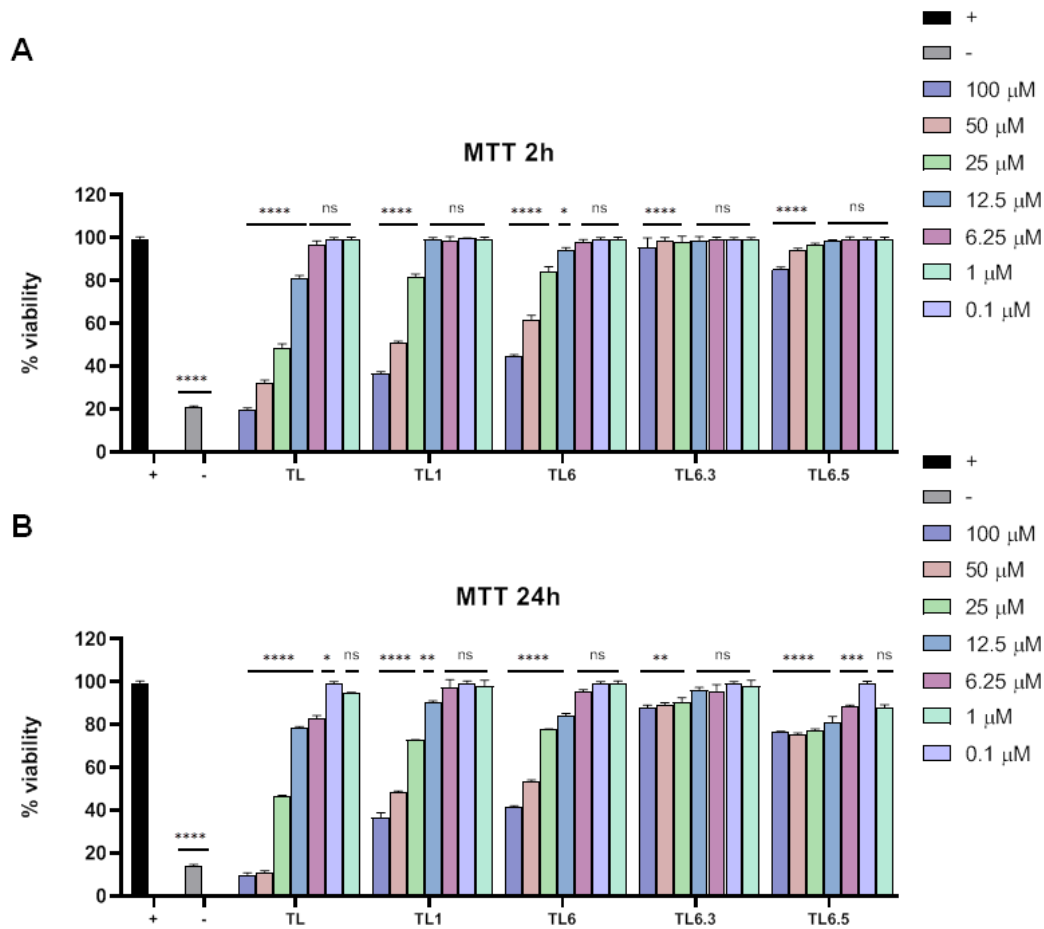
**Figure S1.** Antiviral activity of TL and TL1 against non enveloped RNA virus. Peptides were added in four different “time-of-addition” experiments and their antiviral potential has been analysed against (A) poliovirus and (B) CV-B3. \*\*\*\*  $p < 0.0001$ ; \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ ; ns: non-significant.



**Figure S2.** Peptide toxicity analysis on Vero cells. TL and TL1 toxicity was evaluated by MTT assay after (A) 2 hours and (B) 24 hours peptide treatment and (C) hemolysis assay. \*\*\*\*  $p < 0.0001$ ; \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ , \*  $p < 0.05$ ; ns: non-significant.



**Figure S3.** TL1 analogues toxicity analysis on Vero cells. Peptides toxicity was evaluated by MTT assay after (A) 2 hours and (B) 24 hours peptide treatment and (C) hemolysis assay. \*\*\*\*  $p < 0.0001$ ; \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ ; ns: non-significant.



**Figure S4.** TL, TL1, TL6, TL6.3 and TL6.5 toxicity analysis on PBMCs. Peptides toxicity was evaluated by MTT assay after (A) 2 hours and (B) 24 hours peptide treatment. \*\*\*\*  $p < 0.0001$ ; \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ , \*  $p < 0.1$ ; ns: non-significant.

**Table S1.** CC<sub>50</sub>, IC<sub>90</sub>, IC<sub>50</sub> and TI calculated for HSV-2 and HPIV-3. Concentrations are expressed in  $\mu$ M.

	CC <sub>50</sub>	IC <sub>90</sub>		IC <sub>50</sub>		TI	
		HSV-2	HPIV-3	HSV-2	HPIV-3	HSV-2	HPIV-3
TL1	42.18	16.71	>50.00	8.86	>50.00	4.76	-
TL2	56.52	19.20	>50.00	9.83	>50.00	5.75	-
TL3	>100.00	>50.00	>50.00	>50.00	>50.00	-	-
TL4	60.90	19.02	>50.00	9.61	>50.00	6.34	-
TL5	>100.00	>50.00	>50.00	>50.00	>50.00	-	-
TL6	64.52	6.28	>50.00	0.92	32.35	70.13	1.99
TL7	32.16	11.92	>50.00	3.13	>50.00	10.27	-
TL8	22.32	7.99	>50.00	1.00	40.69	22.32	0.55
TL9	45.92	12.50	>50.00	2.80	40.64	16.40	1.13
TL10	35.47	12.50	>50.00	0.77	>50.00	46.06	-
TL11	24.12	9.76	>50.00	0.58	41.18	41.59	0.59
TL12	8.28	11.68	>50.00	0.54	33.83	15.33	0.24

**Table S2.** CC<sub>50</sub>, IC<sub>90</sub>, IC<sub>50</sub> and TI calculated for HCoV-229E and HCoV-OC43. Concentrations are expressed in  $\mu$ M.

	CC <sub>50</sub>	IC <sub>90</sub>		IC <sub>50</sub>		TI	
		HCoV-229E	HCoV-OC43	HCoV-229E	HCoV-OC43	HCoV-229E	HCoV-OC43
<b>TL1</b>	42.18	30.07	14.98	7.66	7.33	5.51	5.75
<b>TL2</b>	56.52	50.00	24.13	10.56	11.31	5.35	5.00
<b>TL3</b>	>100.00	>50.00	>50.00	>50.00	>50.00	-	-
<b>TL4</b>	60.90	>50.00	27.65	11.74	11.33	5.19	5.38
<b>TL5</b>	>100.00	>50.00	>50.00	>50.00	>50.00	-	-
<b>TL6</b>	64.52	13.06	10.04	2.08	0.97	31.02	66.52
<b>TL7</b>	32.16	>50.00	24.74	6.21	8.55	5.18	3.76
<b>TL8</b>	22.32	50.00	16.30	4.39	2.90	5.08	7.70
<b>TL9</b>	45.92	50.00	29.17	5.39	8.29	8.52	5.54
<b>TL10</b>	35.47	50.00	24.17	0.91	0.96	38.98	36.95
<b>TL11</b>	24.12	50.00	17.41	0.92	5.10	26.22	4.73
<b>TL12</b>	8.28	20.90	13.18	0.74	0.62	11.19	13.35