Supplementary Material

		F	Renilla (RL	U)	1	Firefly (RLU	J)	Firef	ly/Renilla	(F/R)	Mean (F/R)	%			Mean (%)	S.D. (%)
			1				xperimen									
	EV ORF1	200300	201930 520410	193190 502360	300	340 2340	450 2280	0.0015	0.0017	0.0023	0.0018	2	3	4	3	0.7
	MetYPCP	264980	282670	235400	290	320	190	0.0011	0.0045	0.0045	0.0045	2	2	1	2	0.0
	PCP	177860	200810	186360	220	220	350	0.0012	0.0011	0.0019	0.0014	2	2	3	2	0.7
	Met	136510	171450	148370	120	220	220	0.0009	0.0013	0.0015	0.0012	1	2	2	2	0.5
NT	MetY	241570	264610	261210	300	420	270	0.0012	0.0016	0.0010	0.0013	2	3	2	2	0.5
	YPCP	187780	170320	223080	370	260	450	0.0020	0.0015	0.0020	0.0018	3	2	3	3	0.4
	Y	324560	433740	414400	550	690	750	0.0017	0.0016	0.0018	0.0017	3	3	3	3	0.2
	X	233610	352240	365320	290	300	350	0.0012	0.0009	0.0010	0.0010	2	1	2	2	0.3
	MV-V	271880 216550	268710	256650	200	300	220	0.0007	0.0011	0.0009	0.0009	1	2	1	1	0.3
	EV ORF1	558780	222760 579090	207050 550160	14800 24400	13890 25720	11800 22420	0.0683	0.0624	0.0570	0.0626	109 70	100	91 65	100 69	9.1 3.1
	MetYPCP	328990	291910	280530	6050	5840	6230	0.0437	0.0200	0.0408	0.0429	29	32	35	32	3.1
	PCP	214980	231230	233310	8470	9380	8770	0.0394	0.0406	0.0376	0.0392	63	65	60	63	2.4
	Met	209910	201380	191460	15920	14320	13570	0.0758	0.0711	0.0709	0.0726	121	114	113	116	4.5
IFN	MetY	307740	297750	333400	14070	12090	14430	0.0457	0.0406	0.0433	0.0432	73	65	69	69	4.1
	YPCP	245040	252760	215480	15830	15870	14360	0.0646	0.0628	0.0666	0.0647	103	100	107	103	3.1
	Y	485760	520570	427280	25220	24900	19510	0.0519	0.0478	0.0457	0.0485	83	76	73	77	5.1
	X	442440	417760	424150	14950	17650	19960	0.0338	0.0422	0.0471	0.0410	54	68	75	66	10.7
	MV-V	314250	303040	312720	740	930	760	0.0024	0.0031	0.0024	0.0026	4	5	4	4	0.6
	EV	70170	66930	65930	130	80	Experiment 150	2 0.00185	0.0012	0.00228	0.0018	9	6	11	9	2.7
	ORF1	149490	167270	167870	110	140	100	0.000185	0.00012	0.00228	0.0007	4	6 4	3	4	0.6
	MetYPCP	36800	29700	44740	60	60	60	0.00163	0.00202	0.0003	0.0007	- 4	10	7	8	1.7
	PCP	48340	43100	50030	40	90	20	0.00083	0.00209	0.0004	0.0011	4	10	2	5	4.3
NT	Met	29500	28030	30250	40	50	70	0.00136	0.00178	0.00231	0.0018	7	9	11	9	2.4
NI	MetY	46100	44970	50250	110	60	130	0.00239	0.00133	0.00259	0.0021	12	7	13	10	3.3
	YPCP	65090	81310	79390	60	110	140	0.00092	0.00135	0.00176	0.0013	5	7	9	7	2.1
	Y	55110	42850	46580	130	30	60	0.00236	0.0007	0.00129	0.0014	12	3	6	7	4.2
	X	112680	127890	119500	120	130	70	0.00106	0.00102	0.00059	0.0009	5	5	3	4	1.3
	MV-V EV	35540	40000	30880 87250	90 1540	100 1610	20 2080	0.00253	0.0025	0.00065	0.0019	13 94	12 88	3 118	9 100	5.3 15.7
	ORF1	81100 226430	90050 222010	192670	2450	3660	2080	0.01899	0.01788	0.02384	0.02024	53	81	71	69	10.7
	MetYPCP	51430	60800	52650	790	800	740	0.01536	0.01316	0.01406	0.01419	76	65	69	70	5.5
	PCP	46860	43900	46970	970	1190	1270	0.0207	0.02711	0.02704	0.02495	102	134	134	123	18.2
	Met	37880	49790	45390	1180	1190	1190	0.03115	0.0239	0.02622	0.02709	154	118	130	134	18.3
IFN	MetY	54120	57500	65730	1850	2100	2540	0.03418	0.03652	0.03864	0.03645	169	180	191	180	11.0
	YPCP	92860	93870	77410	2280	2420	1860	0.02455	0.02578	0.02403	0.02479	121	127	119	122	4.4
	Y	84040	81300	77870	1870	1660	1840	0.02225	0.02042	0.02363	0.02210	110	101	117	109	8.0
	X	183290 49480	152810 75870	116600 57270	3450 100	2990	2390 60	0.01882	0.01957	0.0205	0.01963	93 10	97 8	101 5	97 8	4.1 2.5
	MV-V					130										
		10100	13010	UT210	100				0.00171	0.00100	0.00100	10	0	0	•	2.0
	EV						Experiment 250	3				4		4		1.4
	EV ORF1	202890	217220	173590 331430	250 1430		Experiment		0.00207	0.00144	0.00158		6 13		5	
		202890	217220	173590	250	450	Experiment 250	3 0.00123	0.00207	0.00144	0.00158	4	6	4	5	1.4
	ORF1 MetYPCP PCP	202890 329300 306760 121330	217220 344920 303370 145490	173590 331430 280160 172800	250 1430 130 130	450 1500 170 170	250 1200 210 290	3 0.00123 0.00434 0.00042 0.00107	0.00207 0.00435 0.00056 0.00117	0.00144 0.00362 0.00075 0.00168	0.00158 0.00410 0.00058 0.00131	4 13 1 3	6 13 2 4	4 11 2 5	5 13 2 4	1.4 1.3 0.5 1.0
NT	ORF1 MetYPCP PCP Met	202890 329300 306760 121330 173750	217220 344920 303370 145490 179090	173590 331430 280160 172800 158860	250 1430 130 130 180	450 1500 170 170 220	Experiment 250 1200 210 290 210	3 0.00123 0.00434 0.00042 0.00107 0.00104	0.00207 0.00435 0.00056 0.00117 0.00123	0.00144 0.00362 0.00075 0.00168 0.00132	0.00158 0.00410 0.00058 0.00131 0.00120	4 13 1 3 3	6 13 2 4 4	4 11 2 5 4	5 13 2 4 4	1.4 1.3 0.5 1.0 0.5
NT	ORF1 MetYPCP PCP Met MetY	202890 329300 306760 121330 173750 284940	217220 344920 303370 145490 179090 361920	173590 331430 280160 172800 158860 361530	250 1430 130 130 180 350	450 1500 170 170 220 440	Experiment 250 1200 210 290 210 460	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124	4 13 1 3 3 4	6 13 2 4 4 4	4 11 2 5 4 4	5 13 2 4 4 4	1.4 1.3 0.5 1.0 0.5 0.1
NT	ORF1 MetYPCP PCP Met MetY YPCP	202890 329300 306760 121330 173750 284940 278550	217220 344920 303370 145490 179090 361920 268710	173590 331430 280160 172800 158860 361530 260290	250 1430 130 130 180 350 370	450 1500 170 170 220 440 220	Experiment 250 1200 210 290 210 460 330	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114	4 13 1 3 3 4 4	6 13 2 4 4 4 3	4 11 2 5 4 4 4	5 13 2 4 4 4 4 4	1.4 1.3 0.5 1.0 0.5 0.1 0.9
NT	ORF1 MetYPCP PCP Met MetY YPCP Y	202890 329300 306760 121330 173750 284940 278550 192870	217220 344920 303370 145490 179090 361920 268710 293460	173590 331430 280160 172800 158860 361530 260290 313440	250 1430 130 130 180 350 370 230	450 1500 170 220 440 220 330	Experiment 250 1200 210 290 210 460 330 440	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00127	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114 0.00124	4 13 1 3 3 4 4 4	6 13 2 4 4 4 3 3	4 11 2 5 4 4 4 4	5 13 2 4 4 4 4 4 4 4	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5
NT	ORF1 MetYPCP PCP Met MetY YPCP Y X	202890 329300 306760 121330 173750 284940 278550 192870 39720	217220 344920 303370 145490 179090 361920 268710 293460 500870	173590 331430 280160 172800 158860 361530 260290 313440 381910	250 1430 130 130 180 350 370 230 20	450 1500 170 220 440 220 330 340	Experiment 250 1200 210 290 210 460 330 440 230	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119 0.00050	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112 0.00068	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00127 0.00140 0.00060	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114 0.00124 0.00059	4 13 1 3 3 4 4 4 4 2	6 13 2 4 4 4 3 3 2	4 11 2 5 4 4 4 4 4 2	5 13 2 4 4 4 4 4 4 2	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3
NT	ORF1 MetYPCP PCP Met MetY YPCP Y	202890 329300 306760 121330 173750 284940 278550 192870	217220 344920 303370 145490 179090 361920 268710 293460	173590 331430 280160 172800 158860 361530 260290 313440	250 1430 130 130 180 350 370 230	450 1500 170 220 440 220 330	Experiment 250 1200 210 290 210 460 330 440	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00127	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114 0.00124	4 13 1 3 3 4 4 4	6 13 2 4 4 4 3 3	4 11 2 5 4 4 4 4	5 13 2 4 4 4 4 4 4 4	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5
NT	ORF1 MetYPCP PCP Met YPCP Y Y X MV-V	202890 329300 306760 121330 173750 284940 278550 192870 39720 392070	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490	250 1430 130 130 180 350 370 230 20 140	450 1500 170 220 440 220 330 340 230	Experiment 250 1200 210 290 210 460 330 440 230 230	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119 0.00050 0.00036	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112 0.00068 0.00049	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00140 0.00060 0.00053	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114 0.00124 0.00059 0.00046	4 13 1 3 3 4 4 4 4 2 1	6 13 2 4 4 4 3 3 2 2 2	4 11 2 5 4 4 4 4 4 4 2 2	5 13 2 4 4 4 4 4 2 1	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3
NT	ORF1 MetYPCP PCP Met YPCP Y Y X MV-V EV	202890 329300 306760 121330 173750 284940 278550 192870 39720 392070 186360	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150	250 1430 130 130 180 350 370 230 20 140 5390	450 1500 170 220 440 220 330 340 230 6380	Experiment 250 1200 210 290 210 460 330 440 230 230 7110	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119 0.00050 0.00036 0.02892	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112 0.00088 0.00049 0.03382 0.03348	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00127 0.00140 0.00060 0.00053 0.03432	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00114 0.00124 0.00059 0.00046 0.03235	4 13 1 3 3 4 4 4 4 2 1 89	6 13 2 4 4 4 3 3 2 2 2 105	4 11 2 5 4 4 4 4 4 2 2 106	5 13 2 4 4 4 4 4 2 1 100	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 0.3 9.2 6.5 2.2
NT	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP PCP	202890 329300 306760 121330 173750 284940 278550 192870 39720 39720 392070 186360 331090 302210 151110	217220 344920 303370 145490 179090 361920 268710 283460 500870 472870 188650 407430 317880 157330	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 411700 370720 167870	250 1430 130 130 180 350 370 230 20 140 5390 11090 11090 1800 4460	450 1500 170 220 2440 220 330 340 230 6380 6380 13640 1470 4000	Experiment 250 1200 210 290 210 460 330 440 230 230 7110 15280 1820 4730	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00133 0.00119 0.00050 0.00036 0.02892 0.003596 0.002951	0.00207 0.00435 0.00056 0.00117 0.00122 0.00082 0.00122 0.00082 0.00049 0.03382 0.00382 0.03382 0.0348 0.00462 0.02542	0.00144 0.00362 0.00075 0.00168 0.00127 0.00127 0.00127 0.00140 0.00053 0.03711 0.03711 0.03711 0.032818	0.00158 0.00410 0.00058 0.00131 0.00124 0.00124 0.00124 0.00059 0.00046 0.03235 0.03270 0.00518 0.002771	4 13 1 3 4 4 4 4 2 1 89 104 18 91	6 13 2 4 4 3 3 2 2 105 103 14 79	4 11 2 5 4 4 4 4 4 2 2 106 115 15 87	5 13 2 4 4 4 4 4 4 2 1 100 107 16 86	1.4 1.3 0.5 1.0 0.5 0.1 0.5 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.2 6.5 2.2 6.4
NT	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP PCP Met	202890 329300 306760 121330 173750 284940 278550 192870 39720 39720 392070 186360 331090 302210 151110 199150	217220 344920 303370 145490 179090 361920 288710 283460 500870 472870 188650 407430 317880 157330 181240	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 411700 370720 167870 173830	250 1430 130 130 350 370 230 140 5390 11090 1800 8380	450 1500 170 220 440 220 340 230 6380 13640 1470 4000 9060	Experiment 250 1200 210 290 210 460 330 230 230 7110 15280 1820 4730 8410	3 0.00123 0.00434 0.0042 0.00107 0.00104 0.00133 0.00133 0.00133 0.00119 0.00050 0.002892 0.00350 0.002951 0.002951	0.00207 0.00435 0.00056 0.00117 0.00122 0.00082 0.00122 0.00049 0.03382 0.03382 0.00499 0.0348 0.004999	0.00144 0.00362 0.00075 0.00168 0.00127 0.00127 0.00140 0.00053 0.03432 0.03711 0.004838 0.04838	0.00158 0.00410 0.0058 0.00131 0.00124 0.00124 0.00124 0.0059 0.0046 0.03235 0.03470 0.00516 0.00516	4 13 1 3 4 4 4 4 2 1 89 104 18 91 130	6 13 2 4 4 3 3 2 2 105 103 14 79 155	4 11 2 5 4 4 4 4 4 2 2 106 115 15 87 150	5 13 2 4 4 4 4 4 4 2 1 100 100 100 16 86 145	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 9.2 6.5 2.2 6.4 12.9
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP PCP Met MetY	202890 329300 121330 173750 284940 278550 192870 39720 392070 188360 331090 302210 151110 199150 404720	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 157330	173590 331430 280150 172800 158860 361530 260290 313440 381910 431490 207150 411700 370720 167870 173830 428310	250 1430 130 130 180 350 230 20 140 5390 11090 1800 4460 8380 7850	450 1500 170 220 330 340 230 6380 13640 1470 4000 7970	Experiment 250 1200 210 290 210 460 230 230 230 230 7110 15280 1820 4730 8410 7740	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00133 0.0019 0.00056 0.02892 0.03350 0.002951 0.04208 0.04208 0.04208	0.00207 0.00435 0.00015 0.00112 0.00123 0.00122 0.00122 0.00082 0.00012 0.00068 0.00049 0.03382 0.03348 0.00462 0.02542 0.04999 0.01909	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00140 0.00060 0.00053 0.03432 0.03711 0.00491 0.02818 0.04838 0.04838	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00124 0.00124 0.00059 0.00059 0.00056 0.03235 0.03470 0.00516 0.02771 0.04682 0.04682 0.04682	4 13 1 3 4 4 4 2 1 89 104 18 91 130 60	6 13 2 4 4 4 3 3 2 2 105 103 14 79 155 59	4 11 2 5 4 4 4 4 2 2 106 115 15 87 150 56	5 13 2 4 4 4 4 4 2 1 100 107 16 86 145 58	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 0.3 0.3 0.3 9.2 6.5 2.2 6.4 12.9 2.1
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP Met MetY YPCP	202890 329300 306760 121330 173750 284940 278550 39720 392070 186360 331090 302210 151110 199150 404720 307040	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 181240 417510 306240	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 431490 370720 167870 173830 428310 338200	250 1430 130 130 180 350 230 20 140 5390 140 5390 11090 1800 4460 8380 7850 6900	450 1500 170 220 440 220 330 340 230 6380 340 230 6380 13640 1470 4000 9060 7970 7350	Experiment 250 1200 210 290 210 460 330 230 230 15280 1820 4730 8410 77140 77990	3 0.00123 0.00424 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119 0.00050 0.002892 0.00350 0.002951 0.002951 0.04208 0.01940 0.02247	0.00207 0.00435 0.00015 0.00117 0.00123 0.00122 0.00122 0.00122 0.00122 0.00082 0.000482 0.03382 0.03382 0.03382 0.02542 0.02542 0.02542 0.01909 0.01909	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00140 0.00040 0.00053 0.03711 0.03711 0.02818 0.04838 0.04838 0.04838	0.00158 0.00410 0.00058 0.00131 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00059 0.00046 0.03270 0.03270 0.03516 0.02771 0.04682 0.01885 0.02337	4 13 1 3 3 4 4 4 4 2 1 89 104 18 91 130 60 69	6 13 2 4 4 4 3 3 2 2 105 103 14 79 155 59 74	4 11 2 5 4 4 4 4 2 2 106 115 15 87 150 56 73	5 13 2 4 4 4 4 4 4 4 4 2 1 1007 107 16 86 145 58 72	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 0.3 0.3 0.3 9.2 6.5 2.2 6.4 12.9 2.1 2.5
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP Met MetY YPCP Y	202890 329300 306760 121330 173750 284940 278550 192870 39720 39720 392070 186860 331090 302210 151110 199150 404720 307040 341030	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 181240 417510 306240 305240	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 431490 207150 431490 207150 167870 173830 428310 338200 344960	250 1430 130 130 350 370 230 20 140 5390 140 5390 11900 4460 8380 7850 6900 10160	450 1500 170 220 440 220 330 340 230 6380 13640 13640 1470 4000 9060 7970 7350 12200	Experiment 250 1200 210 290 210 460 330 7110 15280 1820 4730 8410 77990 10530	3 0.00123 0.00434 0.00042 0.00107 0.00104 0.00123 0.00133 0.00113 0.00119 0.00050 0.00292 0.0350 0.002951 0.04208 0.01247 0.02247	0.00207 0.00435 0.00056 0.00117 0.00123 0.00122 0.00082 0.00112 0.00049 0.03382 0.03382 0.03382 0.03489 0.01909 0.02402 0.02542 0.02542	0.00144 0.00362 0.00075 0.00158 0.00132 0.00127 0.00127 0.00127 0.00140 0.00060 0.00053 0.03432 0.03432 0.03432 0.03432 0.04838 0.04838 0.04838 0.02363 0.02363	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00124 0.00124 0.00124 0.00124 0.00259 0.00246 0.03235 0.03516 0.02771 0.04682 0.02337 0.02316	4 13 1 3 4 4 4 2 1 89 104 18 91 130 60 69 92	6 13 2 4 4 4 3 3 2 2 105 103 14 79 155 59 74 107	4 11 2 5 4 4 4 4 4 2 2 106 115 15 87 150 56 73 94	5 13 2 4 4 4 4 4 4 4 4 2 1 100 100 100 100 106 86 145 58 72 98	1.4 1.3 0.5 1.0 0.5 0.1 0.5 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.2 6.5 6.4 12.9 2.1 2.5 7.8
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP Met MetY YPCP	202890 329300 306760 121330 173750 284940 278550 39720 392070 186360 331090 302210 151110 199150 404720 307040	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 181240 417510 306240	173590 331430 280150 172800 158860 361530 260290 313440 31910 431490 207150 411700 370720 167870 173830 428310 338200 334960 711570	250 1430 130 130 180 350 230 20 140 5390 140 5390 11090 1800 4460 8380 7850 6900	450 1500 170 220 440 220 330 340 230 6380 340 230 6380 13640 1470 4000 9060 7970 7350	Experiment 250 1200 210 290 210 460 330 230 230 15280 1820 4730 8410 77140 77990	3 0.00123 0.00424 0.00042 0.00107 0.00104 0.00123 0.00133 0.00119 0.00050 0.002892 0.00350 0.002951 0.002951 0.04208 0.01940 0.02247	0.00207 0.00435 0.00015 0.00117 0.00123 0.00122 0.00122 0.00122 0.00122 0.00082 0.000482 0.03382 0.03382 0.03382 0.02542 0.02542 0.02542 0.01909 0.01909	0.00144 0.00362 0.00075 0.00132 0.00132 0.00132 0.00127 0.00140 0.00060 0.00053 0.03432 0.03711 0.00491 0.02818 0.04838 0.04838 0.04838 0.01807 0.02363 0.03053 0.03647	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00059 0.00046 0.03270 0.03270 0.00516 0.02771 0.04682 0.01885 0.02337	4 13 1 3 3 4 4 4 4 2 1 89 104 18 91 130 60 69	6 13 2 4 4 4 3 3 2 2 105 103 14 79 155 59 74	4 11 2 5 4 4 4 4 2 2 106 115 15 87 150 56 73	5 13 2 4 4 4 4 4 4 4 4 2 1 1007 107 16 86 145 58 72	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 0.3 0.3 0.3 9.2 6.5 2.2 6.4 12.9 2.1 2.5
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP PCP Met MetY YPCP Y X	202890 329300 121330 173750 284940 278550 192870 39720 39270 192870 39270 192870 39220 186380 331090 332210 151110 199150 404720 307040 341030 606560	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 188650 407430 317880 181240 417510 305240 353540 559470	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 431490 207150 431490 207150 167870 173830 428310 338200 344960	250 1430 130 130 180 350 230 230 230 230 230 230 140 5390 11090 1800 4460 8380 7850 6900 10160 10210	450 1500 170 220 330 220 330 340 230 6380 13640 1470 4000 7970 7350 7970 7350 12200 8720 600	Experiment 250 1200 210 290 210 330 440 230 230 7110 15280 1820 4730 8410 7740 7990 10530 11720	3 0.00123 0.00424 0.00042 0.00042 0.00107 0.00104 0.00123 0.00133 0.00133 0.00133 0.00050 0.000596 0.02892 0.03350 0.00596 0.02921 0.002951 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208 0.04208	0.00207 0.00435 0.00056 0.00123 0.00123 0.00122 0.00068 0.00049 0.00382 0.03348 0.00462 0.02542 0.02542 0.04999 0.022400 0.03451 0.03531	0.00144 0.00362 0.00075 0.00158 0.00132 0.00127 0.00127 0.00127 0.00140 0.00060 0.00053 0.03432 0.03432 0.03432 0.03432 0.04838 0.04838 0.04838 0.02863 0.02363	0.00158 0.00410 0.00058 0.00120 0.00124 0.00124 0.00124 0.00124 0.00124 0.00059 0.00265 0.032470 0.002516 0.02771 0.04682 0.02337 0.021685 0.02337	4 13 3 4 4 4 4 2 1 89 104 18 91 130 60 992 52	6 13 2 4 4 3 3 2 2 105 103 14 79 155 59 74 107 47	4 11 2 5 4 4 4 4 2 2 106 115 15 87 150 56 73 94 51	5 13 2 4 4 4 4 4 4 4 4 1 100 107 166 86 58 72 598 50	1.4 1.3 0.5 1.0 0.5 0.1 0.9 0.5 0.3 0.3 0.3 0.3 0.3 9.2 6.5 2.2 6.4 12.9 2.1 2.5
	ORF1 MetYPCP PCP Met YPCP Y X MV-V EV ORF1 MetYPCP PCP Met MetY YPCP Y X X MV-V EV	202890 329300 306760 121330 173750 284940 278550 192870 39720 39720 392070 186860 331090 302210 151110 199150 404720 307040 341030 605560 540820	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 181240 407430 306240 353540 559470 599960	173590 331430 280160 172800 158860 361530 260290 313440 381910 431490 207150 431490 207150 431490 370720 167870 173830 428310 338200 344960 711570 571560	250 1430 130 130 230 20 140 5390 140 5390 140 6390 4460 8380 7850 6900 10160 10210 510	450 1500 170 220 440 220 330 340 230 6380 13640 13640 1470 4000 9060 7970 7350 12200 8720 600	Experiment 250 1200 210 290 210 460 330 230 230 230 15280 1820 4730 8410 7740 7990 10530 11720 4530 11720 205 205 205 205 205 205 205 2	3 0.00123 0.00424 0.00042 0.00107 0.00104 0.00103 0.00133 0.00133 0.0019 0.00036 0.02892 0.03506 0.02951 0.04208 0.02951 0.04208 0.02951 0.04208 0.02951 0.04208 0.02979 0.01683 0.00044 4 0.00124	0.00207 0.00435 0.00056 0.00117 0.00122 0.00082 0.00049 0.03348 0.0049 0.03348 0.00499 0.03348 0.00499 0.03348 0.02542 0.04999 0.02542 0.04999 0.02542 0.04909 0.02542 0.04909 0.02542 0.01531 0.00100 0.00147	0.00144 0.00362 0.00075 0.00168 0.00132 0.00127 0.00127 0.00127 0.00140 0.00060 0.00053 0.03432 0.03741 0.02818 0.04838 0.04838 0.04838 0.04838 0.04838 0.04807 0.02863 0.01647 0.00080	0.00158 0.00410 0.00058 0.00124 0.00124 0.00124 0.00124 0.00124 0.00059 0.00046 0.032470 0.03470 0.03470 0.03470 0.03470 0.034682 0.02337 0.03161 0.01621 0.0092	4 13 1 3 3 4 4 4 4 4 4 4 2 1 89 104 189 104 189 104 189 104 189 104 189 104 189 104 189 104 189 104 189 104 189 104 180 180 191 180 180 191 191 191 191 191 191 191 191 191 19	6 13 2 4 4 4 4 3 3 2 2 105 103 14 105 59 74 107 74 107 47 3 2	4 11 2 5 4 4 4 4 4 4 4 4 4 2 2 1006 115 15 56 73 94 56 73 94 2 2	5 13 2 4 4 4 4 4 4 4 4 2 1 100 100 100 100 100 106 86 145 58 50 3 3	1.4 1.3 0.5 1.0 0.5 0.1 0.5 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3
	ORF1 MetYPCP PCP Met MetY YPCP Y X MV-V EV ORF1 MetYPCP PCP Met MetY YPCP Y X MV-V EV ORF1	202890 329300 121330 173750 284940 278550 192870 39720 39720 392200 186380 331090 302210 151110 404720 307040 341030 606560 540820 137220 189840	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 157330 407430 317880 157330 181240 417510 305240 353540 569470 599960 149460 186430	173590 331430 280150 172800 158860 361530 260290 313440 381910 431490 207150 411700 370720 167870 428310 338200 338200 338200 711570 571550	250 1430 130 130 180 350 20 230 20 140 5390 11090 1800 4460 8380 7850 6900 10160 10210 510	450 1500 170 220 330 340 230 6380 13640 1470 4000 7970 7350 8720 600 8720 600	Experiment 250 1200 210 290 210 330 440 230 230 7110 15280 180 11720 460 Experiment 180 2210	3 0.00123 0.00434 0.000422 0.000107 0.00104 0.00103 0.00103 0.00113 0.00113 0.00119 0.00050 0.00050 0.000596 0.002892 0.03350 0.00294 0.02247 0.02247 0.02247 0.02247 0.02247 0.02959 0.02683 0.00944 4 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00124 0.00125 0.00125 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.00259 0.	0.00207 0.00435 0.00056 0.00123 0.00123 0.00122 0.000122 0.000122 0.00049 0.00049 0.00382 0.03348 0.00462 0.03348 0.00462 0.02542 0.02542 0.02542 0.02543 0.01531 0.00147 0.02143	0.00144 0.00362 0.00075 0.00132 0.00132 0.00127 0.00140 0.00060 0.00053 0.00491 0.02818 0.0493 0.02818 0.0493 0.0283 0.01827 0.0283 0.01867 0.02053 0.01647 0.00080 0.00132 0.00132 0.00132	0.00158 0.00410 0.00058 0.00131 0.00120 0.00124 0.00124 0.00124 0.00124 0.00125 0.00145 0.00259 0.002771 0.00516 0.02771 0.004682 0.02337 0.02711 0.04682 0.02337 0.02155 0.02315 0.02155 0.02155 0.02155 0.02155 0.001555	4 13 1 3 3 4 4 4 2 1 89 104 18 91 130 60 92 92 52 3 2 19	6 13 2 4 4 4 3 2 105 103 14 79 155 59 74 107 47 3 2 37	4 11 2 5 5 4 4 4 4 4 2 2 106 115 15 87 150 56 87 150 56 73 94 51 2 2 20	5 13 2 4 4 4 4 4 4 4 4 4 4 1 100 107 166 86 58 72 58 72 98 50 3 3	1.4 1.3 0.5 1.0 0.5 1.0 0.5 0.3 0.3 0.2 6.4 12.9 2.1 2.5 0.3 0.2 10.0
	ORF1 MetYPCP PCP Met MetY YPCP Y X MV-V EV ORF1 MetYPCP Y X MV-V EV ORF1 MetYPCP	202890 329300 121330 173750 284940 278550 192870 39720 392070 188360 331090 302210 151110 188360 331090 302210 151110 199150 404720 307040 341030 606550 540820	217220 344920 303370 145490 179090 361920 268710 293460 500870 472870 188650 407430 317880 407430 317880 407430 317880 407430 317880 407430 317880 407430 317880 407430 35540 5599470 559940 188430 188430 188430	173590 331430 280150 172800 158860 361530 260290 313440 381910 431490 207150 411700 370720 167870 173830 428310 338200 344960 711570 571560 135880 187930 147810	250 1430 130 130 180 350 20 20 20 20 20 5390 11090 1800 4460 8380 8380 7850 6900 10160 10210 510 510	450 1500 170 170 220 330 220 330 230 6380 13640 1470 6380 13640 1470 4000 7970 7350 12200 8720 600 220 4070 260	Experiment 250 1200 210 210 210 330 440 230 230 230 230 230 7110 15280 1820 4730 8410 7740 7990 10530 11720 460 Experiment 180 2210 270	3 0.00123 0.00424 0.000422 0.00042 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Table S1. Raw data from the luciferase reporter assays presented in Figure 1c. Mean ratios between firefly and *Renilla* luciferase activities were calculated (F/R) and are presented as percentages (%) of the treated EV control in 4 independent experiments. Mean values and standard deviation (S.D.) are presented for not-treated (NT) and IFN- β -treated (IFN) conditions.

			Renilla (RL	U)		Firefly (RLU	J)	Firef	y/Renilla	(F/R)	Mean (F/R)	%		Mean (%)	S.D. (%)	
							Experime	nt 1			(inty				1.47	
	EV	200300	201930	193190	300	340	450	0.0015	0.0017	0.0023	0.0018	2	3	4	3	0.7
	MetYPCP-G3	264980	282670	235400	290	320	190	0.0011	0.0011	0.0008	0.0010	2	2	1	2	0.3
	PCP-G3	177860	200810	186360	220	220	350	0.0012	0.0011	0.0019	0.0014	2	2	3	2	0.7
NT	MetYPCP-G1	202530	207220	222490	360	310	300	0.0018	0.0015	0.0013	0.0015	3	2	2	2	0.3
	PCP-G1	148850	212410	210900	260	260	360	0.0017	0.0012	0.0017	0.0016	3	2	3	2	0.5
	MV-V	271880	268710	256650	200	300	220	0.0007	0.0011	0.0009	0.0009	1	2	1	1	0.3
	EV	216550	222760	207050	14800	13890	11800	0.0683	0.0624	0.0570	0.0626	109	100	91	100	9.1
	MetYPCP-G3	328990	291910	280530	6050	5840	6230	0.0184	0.0200	0.0222	0.0202	29	32	35	32	3.1
IFN	PCP-G3	214980	231230	233310	8470	9380	8770	0.0394	0.0406	0.0376	0.0392	63	65	60	63	2.4
	MetYPCP-G1	268250	245390	287010	10810	8390	10550	0.0403	0.0342	0.0368	0.0371	64	55	59	59	4.9
	PCP-G1	245420	228780	221960	16700	18660	14520	0.0680	0.0816	0.0654	0.0717	109	130	105	115	13.8
	MV-V	314250	303040	312720	740	930	760	0.0024	0.0031	0.0024	0.0026	4	5	4	4	0.6
100 0024 0.024 0.024 0.024 0.024 4.024 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.025 4.005 4.025 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.005 4.0																
	EV	70170	66930	65930	130	80	150	0.00185	0.0012	0.00228	0.0018	9	6	11	9	2.7
	MetYPCP-G3	36800	29700	44740	60	60	60	0.00163	0.00202	0.00134	0.0017	8	10	7	8	1.7
	PCP-G3	48340	43100	50030	40	90	20	0.00083	0.00209	0.0004	0.0011	4	10	2	5	4.3
NT	MetYPCP-G1	45740	37020	43580	60	90	100	0.00131	0.00243	0.00229	0.0020	6	12	11	10	3.0
	PCP-G1	60430	54670	61390	80	70	70	0.00132	0.00128	0.00114	0.0012	7	6	6	6	0.5
	MV-V	35540	40000	30880	90	100	20	0.00132	0.00128	0.00065	0.0012	13	12	3	9	5.3
<u> </u>	EV	35540 81100	90050	30880	90 1540	1610	2080	0.00253	0.0025	0.00065	0.0019	94	88	3 118	100	5.3
	EV MetYPCP-G3	51430	60800	52650	790	800	740	0.01899	0.01788	0.02384	0.02024	94	65	69	70	5.5
IFN	PCP-G3	46860	43900	46970	970	1190	1270	0.0207	0.02711	0.02704	0.02495	102	134	134	123	18.2
	MetYPCP-G1	54080	60920	56870	1440	1730	1420	0.02663	0.0284	0.02497	0.02666	132	140	123	132	8.5
	PCP-G1	59910	66630	63450	1380	1420	1780	0.02303	0.02131	0.02805	0.02413	114	105	139	119	17.3
	MV-V	49480	75870	57270	100	130	60	0.00202	0.00171	0.00105	0.00159	10	8	5	8	2.5
								nt 3								
	EV	202890	217220	173590	250	450	250	0.00123	0.00207	0.00144	0.00158	4	6	4	5	1.4
	MetYPCP-G3	306760	303370	280160	130	170	210	0.00042	0.00056	0.00075	0.00058	1	2	2	2	0.5
NT	PCP-G3	121330	145490	172800	130	170	290	0.00107	0.00117	0.00168	0.00131	3	4	5	4	1.0
	MetYPCP-G1	247460	244000	277580	160	130	180	0.00065	0.00053	0.00065	0.00061	2	2	2	2	0.2
	PCP-G1	355340	499600	352410	260	360	240	0.00073	0.00072	0.00068	0.00071	2	2	2	2	0.1
	MV-V	392070	472870	431490	140	230	230	0.00036	0.00049	0.00053	0.00046	1	2	2	1	0.3
	EV	186360	188650	207150	5390	6380	7110	0.02892	0.03382	0.03432	0.03235	89	105	106	100	9.2
	MetYPCP-G3	302210	317880	370720	1800	1470	1820	0.00596	0.00462	0.00491	0.00516	18	14	15	16	2.2
	PCP-G3	151110	157330	167870	4460	4000	4730	0.02951	0.02542	0.02818	0.02771	91	79	87	86	6.4
IFN	MetYPCP-G1	335600	282950	299520	3110	3240	3230	0.00927	0.01145	0.01078	0.01050	29	35	33	32	3.5
	PCP-G1	412860	393580	372060	6850	5680	5980	0.01659	0.01443	0.01607	0.01570	51	45	50	49	3.5
	MV-V	540820	599960	571560	510	600	460	0.00094	0.00100	0.00080	0.00092	3	3	2	3	0.3
								nt 4								
	EV	137220	149460	135880	170	220	180	0.00124	0.00147	0.00132	0.0013452	2	2	2	2	0.2
	MetYPCP-G3	127670	126210	147810	130	260	270	0.00102	0.00206	0.00183	0.001635	2	3	3	3	0.9
	PCP-G3	91050	101560	84190	150	170	130	0.00165	0.00167	0.00154	0.0016218	3	3	3	3	0.1
NT	MetYPCP-G1	298560	298620	303850	310	240	210	0.00103	0.0008	0.00069	0.0008444	2	1	1	1	0.1
	PCP-G1	121710	112650	111290	300	310	440	0.00104	0.00275	0.00395	0.0030568	4	5	7	5	1.3
	MV-V	134080	12650	127210	180	160	200	0.00246	0.00275	0.00395	0.0013997	2	2	3	2	0.3
<u> </u>	EV	170650	124570	149520	9170	9290	10250	0.00134	0.05467	0.06855	0.0013997	2 91	93	116	100	14.1
	EV MetYPCP-G3	170650	169920		9170 5190	9290 5020	10250	0.05374	0.05467	0.06855		91 64	93 61	79	100 68	14.1 9.6
				121100	5190 4750						0.0402845		60		68	9.6
IFN	PCP-G3	111450	105190	112120		3720	4160	0.04262	0.03536	0.0371	0.0383626	72		63		
	MetYPCP-G1	312570	304910	274430	10090	8540	9880	0.03228	0.02801	0.036	0.032097	55	47	61	54	6.8
	PCP-G1	125860	122480	113670	11860	12790	9390	0.09423	0.10443	0.08261	0.0937548	160	177	140	159	18.5
	MV-V	132770	136310	128020	460	640	520	0.00346	0.0047	0.00406	0.0040739	6	8	7	7	1.0
Experiment 5																
NT	EV	34730	61960	53620	60	250	140	0.00173	0.00403	0.00261	0.0027911	2	5	3	3	1.4
	MetYPCP-G3	106760	106090	114750	180	200	240	0.00169	0.00189	0.00209	0.0018876	2	2	3	2	0.3
	PCP-G3	59960	57460	69510	140	100	160	0.00233	0.00174	0.0023	0.0021257	3	2	3	3	0.4
	MetYPCP-G1	55420	54140	62980	200	250	280	0.00361	0.00462	0.00445	0.0042241	4	6	5	5	0.7
	PCP-G1	46030	54840	50000	190	250	150	0.00413	0.00456	0.003	0.0038955	5	6	4	5	1.0
	MV-V	63230	55010	51370	120	100	100	0.0019	0.00182	0.00195	0.0018874	2	2	2	2	0.1
	EV	70050	69220	61310	5650	5120	5390	0.08066	0.07397	0.08791	0.0808459	100	91	109	100	8.6
	MetYPCP-G3	130380	125220	99210	4130	3710	3680	0.03168	0.02963	0.03709	0.0327992	39	37	46	41	4.8
	PCP-G3	84470	70890	55510	4420	4310	3980	0.05233	0.0608	0.0717	0.0616078	65	75	89	76	12.0
IFN	MetYPCP-G1	68850	72360	60140	5070	5070	4430	0.07364	0.07007	0.07366	0.0724554	91	87	91	90	2.6
	PCP-G1	66090	56780	53050	5350	3860	4170	0.08095	0.06798	0.07861	0.0758457	100	84	97	94	8.5
	MV-V	58160	49940	53740	750	550	670	0.08085	0.01101	0.01247	0.0121254	16	14	15	15	1.2
	m¥-V	50100	45840	00740	100	330	010	0.0128	0.01101	0.01247	0.0121204	10	19	10	10	1.4

Table S2. Raw data from the luciferase reporter assays presented in Figure 6b. Mean ratios between firefly and *Renilla* luciferase activities were calculated (F/R) and are presented as percentages (%) of the treated EV control in 5 independent experiments. Mean values and standard deviation (S.D.) are presented for not-treated (NT) and IFN-β-treated (IFN) conditions.

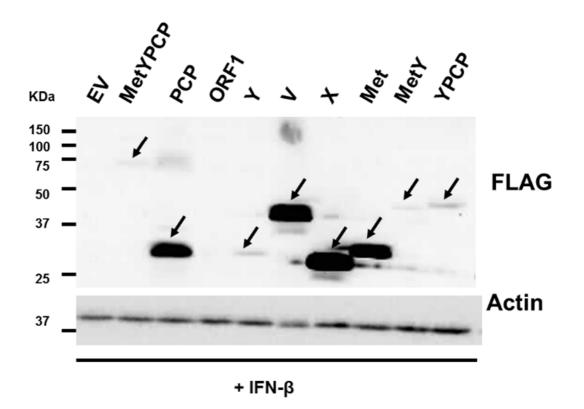


Figure S1. Expression of FLAG-tagged full-length and domains of ORF1 in co-transfected 293T cells. Cell lysates generated for the luciferase reporter assay (Figure 1c) were analysed by immunoblotting using an anti-FLAG antibody. Bands corresponding to the different FLAG-tagged proteins are shown by arrows. Note that ORF1 was not detected. Actin served as loading control.

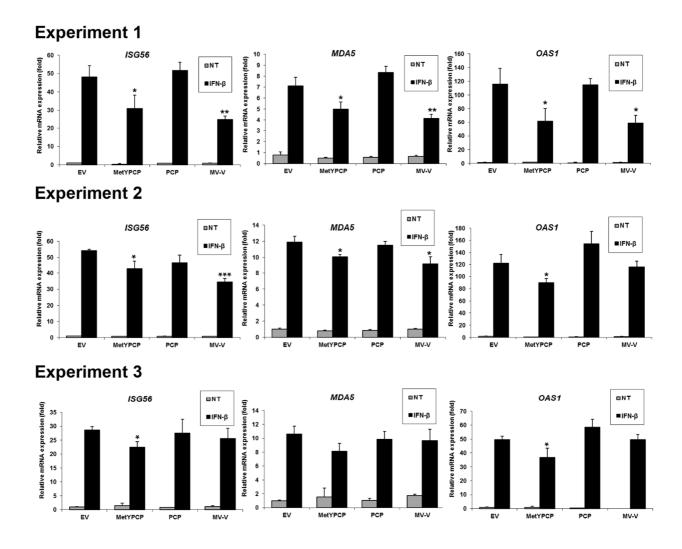


Figure S2. Relative expression of ISG56, MDA5 and OAS1 mRNA determined by RT-qPCR for each of the 3 independent experiments presented in Figure 2. Data are presented as fold induction (+ standard deviations) relative to the non-stimulated EV control. *, P < 0.005; ***, P < 0.0005; ***, P < 0.0005 compared to EV control for treated samples (unpaired t tests).

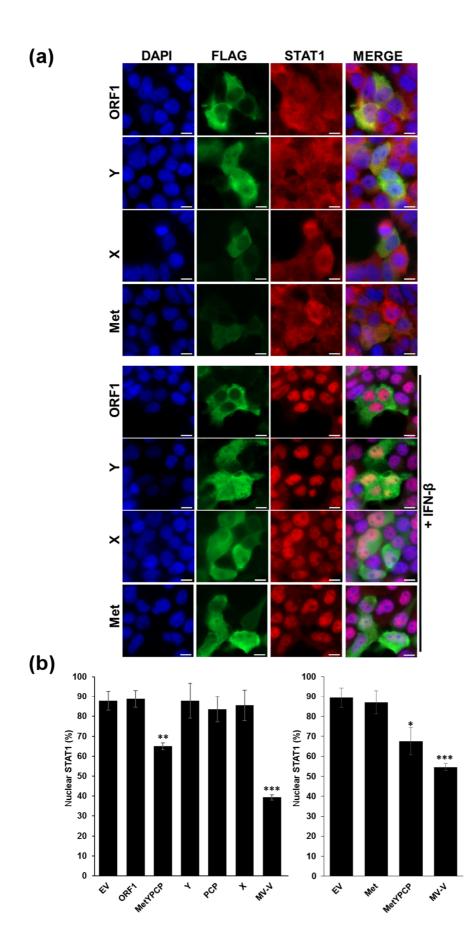


Figure S3. Expression of ORF1, Y, X and Met of HEV ORF1 has no impact on STAT1 nuclear translocation upon IFN-β treatment. (a) 293T cells were transfected with a pCINeo-3xFLAG empty vector (EV) or a plasmid coding for ORF1, Y, X or Met fused to a FLAG tag. Twenty four h post-transfection, cells were left untreated or stimulated for 30 min with 1000 IU/ml of IFN-β. Cells were then washed, fixed and stained with primary antibodies raised against STAT1 and FLAG, followed by fluorescent dye-conjugated secondary antibodies. Intracellular localization of DAPI-stained nuclei (blue), FLAG (green) and STAT1 (red) was visualized by microscopy (magnification, x630). Scale bars, 10 μm. (b) STAT1 localization was visualized after immunostaining as described in (a) in 293T cells transfected with a pCINeo-3xFLAG empty vector (EV) or a plasmid coding for ORF1, MetYPCP, PCP, X, Y, Met or MV-V fused to a FLAG tag. For each condition, STAT1 localization was determined in 48 to 181 cells expressing the corresponding FLAG-tagged protein (except for the EV control for which 356 to 384 cells were randomly assessed). The mean percentage (± standard deviation) of cells showing a predominant nuclear localization of STAT1 from 3 independent experiments is shown. *p<0.05; **p<0.005; ***p<0.0005 compared to EV control for treated samples (unpaired t tests). (a-b) Data presented for the Met domain are from a different set of experiments than the one presented for ORF1, Y and X.

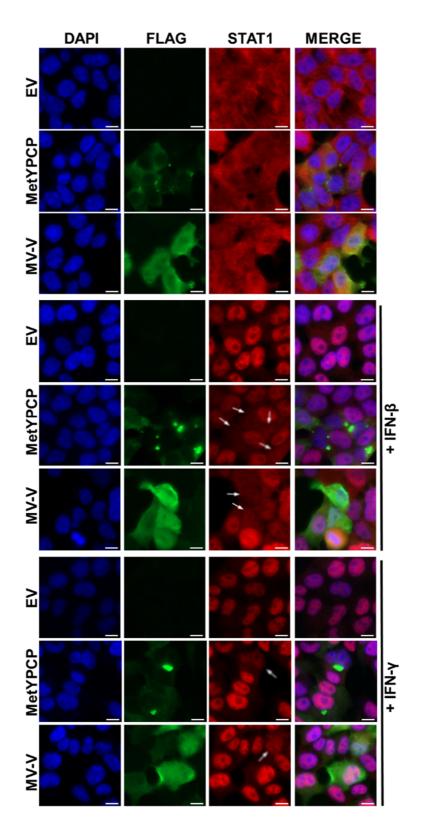


Figure S4. Effect of MetYPCP of HEV ORF1 on STAT1 translocation in response to IFN-II. 293T cells were transfected with a pCINeo-3×FLAG empty vector (EV) or a plasmid coding for MetYPCP or MV-V fused to a 3xFLAG tag. Twenty four h post-transfection, cells were stimulated for 30 min with 1000 IU/ml of IFN-β or 250 ng/ml of IFN-γ. Cells were then washed, fixed and stained with primary antibodies raised against STAT1 and FLAG, followed by fluorescent dye-conjugated secondary antibodies. Cells showing diffuse cytoplasmic/nuclear localisation of STAT1 upon IFN-β treatment are indicated by arrows. Scale bars, 10 μm.

MetYPCP-G1	1	MEAHQFIKAPGITTAIEQAALAAANSALANAVVVRPFLSHQQIEILINLM	50
MetYPCP-G3	1		50
MetYPCP-G1	51	QPRQLVFRPEVFWNHPIQRVIHNELELYCRARSGRCLEIGAHPRSINDNP	100
MetYPCP-G3	51	QPRQLVFRPEVLWNHPIQRVIHNELEQYCRARAGRCLEVGAHPRSINDNP	100
MetYPCP-G1	101	NVVHRCFLRPVGRDVQRWYTAPTRGPAANCRRSALRGLPAADRTYCFDGF	150
MetYPCP-G3	101	NVLHRCFLRPVGRDVQRWYSAPTRGPAANCRRSALRGLPPVDRTYCFDGF	150
MetYPCP-G1	151	SGCNFPAETGIALYSLHDMSPSDVAEAMFRHGMTRLYAALHLPPEVLLPP	200
MetYPCP-G3	151	SRCAFAAETGIALYSLHDLWPSDVAEAMARHGMTRLYAALHLPPEVLLPP	200
MetYPCP-G1	201	GTYRTASYLLIHDGRRVVVTYEGDTSAGYNHDVSNLRSWIRTTKVTGDHP	250
MetYPCP-G3	201	GTYHTTSYLLIHDGNRAVVTYEGDTSAGYNHDVSILRAWIRTTKIVGDHP	250
MetYPCP-G1	251	LVIERVRAIGCHFVLLLTAAPEPSPMPYVPYPRSTEVYVRSIFGPGGTPS	300
MetYPCP-G3	251	LVIERVRAIGCHFVLLLTAAPEPSPMPYVPYPRSTEVYVRSIFGPGG <mark>S</mark> PS	300
MetYPCP-G1	301	LFP <mark>TS</mark> CSTKSTFHAVP T HIWDRLMLFGATLDDQAFCCSRLMTYLRGISYK	350
MetYPCP-G3	301	LFP <mark>SA</mark> CSTKSTFHAVPVHIWDRLMLFGATLDDQAFCCSRLMTYLRGISYK	350
MetYPCP-G1	351	VTVGTLVANEGWNASEDALTAVITAAYLTICHQRYLRTQAISKGMRRLER	400
MetYPCP-G3	351	VTVGALVANEGWNASEDALTAVITAAYLTICHQRYLRTQAISKGMRRLEV	400
MetYPCP-G1	401	EHAQKFITRLYSWLFEKSGRDYIPGRQLEFYAQCRRWLSAGFHLDPRVLV	450
MetYPCP-G3	401	EHAQKFITRLYSWLFEKSGRDYIPGRQL <mark>Q</mark> FYAQCRRWLSAGFHLDPRVLV	450
MetYPCP-G1	451	FDESAPCHCRTAIRKAFSKFCCFMKWLGQECTCFLQPAEGVVGDQGHDNE :. . :::	500
MetYPCP-G3	451	FDEAVPCRCRSFLKKVAGKFCCFMKWLGQECTCFLEPAEGLVGDCGHDNE	500
MetYPCP-G1	501	AYEGSDVDPAESAISDISGSYVVPGTALQPLYQALDLPAEIVARAGRLTA	550
MetYPCP-G3	501	AYEGSEVDPAEPAHLDVSGTYAVHGRQLEALYRALNIPDDIAARASRLTA	550
MetYPCP-G1	551	TVKVSQVDGRIDCETLLGNKTFRTSFVDGAVLETNGPERHNL 592	
MetYPCP-G3	551	TVELAASPGRLECRTVLGNKTFRTSITDGAHLEANGPEQYVL 592	

Figure S5. Alignment of the amino acid sequence of MetYPCP from genotypes 1 and 3. The amino acid sequence of MetYPCP from genotype 1 (MetYPCP-G1) is 86% identical to the one of MetYPCP from genotype 3 (MetYPCP-G3). Pairwise Sequence Alignment (PROTEIN) EMBOSS Needle was used (<u>https://www.ebi.ac.uk/Tools/psa/emboss_needle/</u>). Different amino acids are highlighted in red. : indicates similar amino acids.

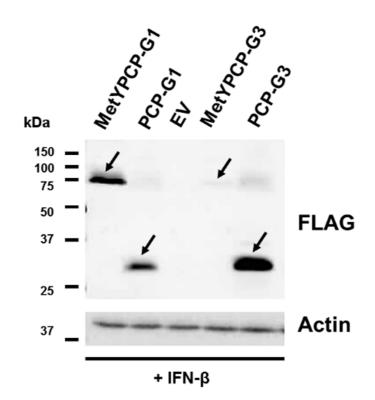


Figure S6. Expression of FLAG-tagged MetYPCP and PCP from genotypes 1 and 3 in co-transfected 293T cells. Cell lysates generated for the luciferase reporter assay (Figure 6b) were analysed by immunoblotting using an anti-FLAG antibody. Bands corresponding to the different FLAG-tagged proteins are shown by arrows. Actin served as loading control.

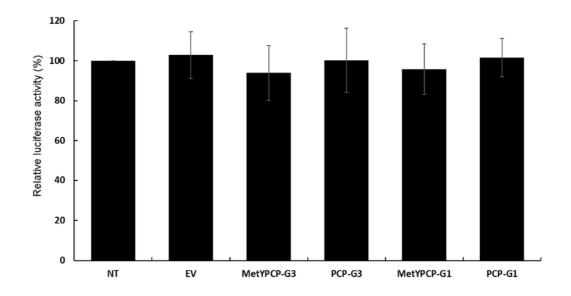


Figure S7. Cell viability assay in cells expressing MetYPCP and PCP from HEV-1 and HEV-3. 293T cells were transfected or not (NT) with a pCINeo-3xFLAG empty vector (EV) or a plasmid coding for MetYPCP and PCP from genotype 1 and 3 fused to a 3xFLAG tag. Forty h after transfection, cells were lysed and cell viability determined using a luminescent-based assay. Luciferase activities (± standard deviations) are expressed as percentage relative to non-transfected cells. No significant difference was found between the cells transfected with the pCINeo-3xFLAG empty vector and the one transfected with the plasmids coding for MetYPCP or PCP from HEV-1 and HEV-3 (unpaired t tests). Results represent the mean of 3 independent experiments performed in triplicate.

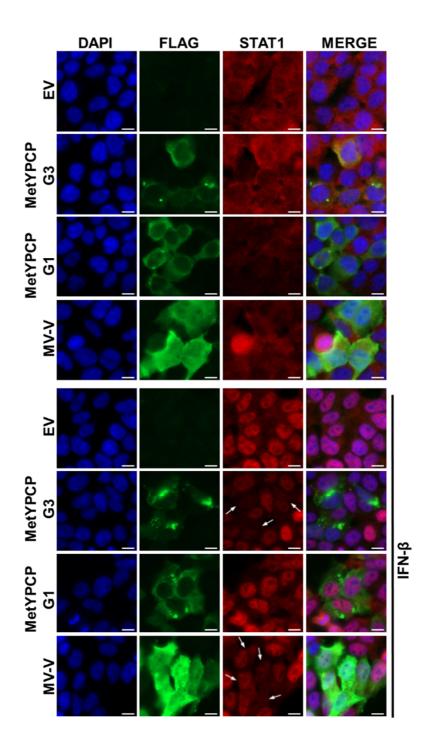


Figure S8. Effect of MetYPCP from HEV-1 on STAT1 translocation. 293T cells were transfected with a pCINeo-3xFLAG empty vector (EV) or a plasmid coding for MetYPCP from HEV-1 or HEV-3 or MV-V fused to a 3xFLAG tag. Twenty-four h post-transfection, cells were stimulated for 30 min with 1000 IU/ml of IFN- β . Cells were then washed, fixed and stained with primary antibodies raised against STAT1 and FLAG, followed by fluorescent dye-conjugated secondary antibodies. Cells showing diffuse STAT1 cytoplasmic/nuclear localisation upon IFN- β treatment are indicated by arrows. Scale bars, 10 µm.