

Figure 4—source data 1. List of ten highest % frequency non-synonymous mutations for each proteostasis environment and passage.

HSF1-Activated									
Passage 2		Passage 9		Passage 11		Passage 19		Passage 23	
Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.
NS1 F150S	41	HA N144T	88	HA N144T	98	HA M246I	100	HA M246I	100
HA N144T	30	HA V242I	87	HA V242I	97	HA V242I	100	HA V242I	100
PA H452Q	25	HA M246I	86	HA M246I	97	HA N144T	100	HA N144T	100
HA M246I	24	PB2 F14S	76	<i>PB2 F14S</i>	96	PB2 F14S	100	PB2 F14S	100
HA N262K	17	NS1 F150S	37	PA H452Q	26	NP G384R	94	<i>NP G384R</i>	100
HA V242I	11	PA H452Q	34	NS1 F150S	26	NP D101G	55	NP D101G	91
<i>HA N142K</i>	4	PA V44A	16	<i>NP G384R</i>	23	M1 K174R	43	M1 K174R	89
<i>HA E402G</i>	4	<i>NP G384R</i>	13	PB1 Y49*	15	PB1 I517V	41	PB1 Y49*	64
NS1 R37G	3	PB2 E2K	12	PA V44A	15	PB1 Y49*	33	PB1 I517V	60
NS1 N127T	2	PB1 E697K	10	NP D480N	11	PB1 H456N	26	PA E604G	26
Baseline									
Passage 2		Passage 9		Passage 11		Passage 19		Passage 23	
Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.
NS1 F150S	36	HA N144T	73	HA N144T	78	HA V242I	100	HA V242I	100
PA H452Q	34	HA V242I	72	HA V242I	78	HA M246I	100	HA M246I	100
HA N144T	26	HA M246I	72	HA M246I	77	HA N144T	100	PB2 F14S	100
HA M246I	21	PA H452Q	49	PA H452Q	54	<i>PB2 F14S</i>	100	HA N144T	100
HA N262K	20	PB1 V660F	46	PB1 V660F	51	NP D101N	80	NP G384R	94
HA N142K	7	PA N359T	22	PA N359T	30	HA I538T	78	PA M12I	93
NS1 R118K	6	NS1 F150S	17	NP D101N	26	PA M12I	63	NP D101N	88
PB1-F2 R21K	4	PB1 F700S	15	PB2 F14S	22	<i>PA H452Q</i>	60	HA I538T	80
HA G140D	4	NP G384R	13	NS1 R118K	22	HA G349S	57	PA E15K	64
NP V100I	3	NP D101N	13	PB1 F700S	18	NP G384R	54	<i>PA H452Q</i>	63
Hsp90-Inhibited									
Passage 2		Passage 9		Passage 11		Passage 19		Passage 23	
Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.	Mutation	Freq.
HA N144T	32	<i>HA N144T</i>	53	<i>HA N144T</i>	70	<i>HA M246I</i>	100	HA M246I	100
PA H452Q	28	HA V242I	49	<i>HA V242I</i>	69	<i>HA V242I</i>	100	HA N144T	100
NS1 F150S	25	<i>HA M246I</i>	48	<i>HA M246I</i>	68	<i>HA N144T</i>	100	HA V242I	100
HA M246I	19	PA H452Q	41	PA H452Q	46	HA A492V	99	<i>M1 K174R</i>	100
HA N262K	18	NP N319K	28	NP N319K	39	HA Y249H	98	HA Y249H	99
HA N142K	12	NS1 R118K	18	HA Y249H	35	<i>PB2 F14S</i>	95	HA A492V	99

NS1 I182T; NEP S27P	9	NS1 I182T; NEP S27P	18	NS1 R118K	26	M1 K174R	86	<i>PB2 F14S</i>	98
NS1 R118K	9	HA Y249H	15	NS1 I182T; NEP S27P	26	<i>NP N319K</i>	81	<i>NP N319K</i>	96
<i>HA E402G</i>	5	PA D3Y	11	HA A492V	19	PA H452Q	71	PA H452Q	93
M2 A30T	4	NS1/NEP V6L	11	NS1/NEP V6L	17	<i>M1 T239A</i>	61	HA R241G	83

*Bolted mutations were observed in 3/3 biological replicates; italicized mutations were observed in 2/3 biological replicates; codon number is in parentheses.