

Table S1: Mutation distribution data for experiments presented.

# clones with n mutations	WT	A372V	S299T	WT ribavirin	A372V ribavirin	S299T ribavirin
7 mutations	0	0	0	1	0	3
6 mutations	0	0	0	1	1	2
5 mutations	0	0	0	2	0	7
4 mutations	0	0	0	5	3	4
3 mutations	1	0	5	9	6	10
2 mutations	6	2	11	15	15	18
1 mutations	40	14	70	25	29	14
0 mutations	95	68	92	13	20	10
Total mutations	55	18	107	125	95	164
Total # clones	142	84	178	71	74	68
Total nt sequenced	121,978	72,156	152,902	60,989	63,566	58,412
Mutations/10⁴ nt	4.51	2.49	7.00	20.50	14.94	28.08

# clones with n mutations	WT amiloride	A372V amiloride	S299T amiloride	WT EIPA	A372V EIPA	S299T EIPA
7 mutations	0	0	0	0	0	0
6 mutations	0	0	0	0	0	0
5 mutations	1	0	0	0	0	0
4 mutations	0	1	1	0	0	0
3 mutations	10	2	2	4	1	4
2 mutations	15	9	13	10	3	8
1 mutations	38	39	29	27	16	24
0 mutations	64	75	48	40	51	45
Total mutations	103	67	65	59	25	52
Total # clones	128	126	93	81	71	81
Total nt sequenced	109,952	108,234	79,887	69,579	60,989	69,579
Mutations/10⁴ nt	9.37	6.19	7.89	8.48	2.49	7.47

# clones with n mutations	WT MIA	WT benzamil	polio WT	polio G64S	polio WT amiloride	polio G64S amiloride
7 mutations	0	0	0	0	0	0
6 mutations	1	0	0	0	0	0
5 mutations	0	0	0	0	0	0
4 mutations	1	0	0	0	0	0
3 mutations	3	1	2	0	6	4
2 mutations	12	7	10	5	12	10
1 mutations	14	26	36	35	34	34
0 mutations	36	45	74	88	46	64
Total mutations	57	43	62	45	72	66
Total # clones	67	79	122	128	96	112
Total nt sequenced	57,553	67,861	107,848	113,152	84,864	99,008
Mutations/10⁴ nt	9.90	6.34	5.75	3.97	8.48	7.47

# clones with n mutations	WT NaCl	A372V NaCl	S299T NaCl	WT CaCl ₂	A372V CaCl ₂	S299T CaCl ₂
7 mutations	0	0	0	0	0	0
6 mutations	0	0	0	0	0	0

5 mutations	0	0	0	0	0	0
4 mutations	0	0	0	0	0	0
3 mutations	0	0	3	0	0	1
2 mutations	4	1	10	4	0	13
1 mutations	36	27	41	40	30	37
0 mutations	54	64	40	42	64	41
Total mutations	44	29	70	48	30	66
Total # clones	94	92	94	90	94	92
Total nt sequenced	103,400	101,200	103,400	99,000	103,400	92,000
Mutations/10⁴ nt	4.26	2.87	6.77	4.85	2.90	7.17

# clones with n mutations	WT MgCl ₂	A372V MgCl ₂	S299T MgCl ₂	WT MnCl ₂	A372V MnCl ₂	S299T MnCl ₂
7 mutations	1	0	0	0	0	0
6 mutations	0	0	0	0	0	0
5 mutations	2	0	3	0	0	0
4 mutations	2	0	0	1	0	1
3 mutations	4	1	1	0	1	0
2 mutations	15	8	12	11	5	15
1 mutations	35	20	26	21	37	25
0 mutations	37	53	52	22	47	40
Total mutations	102	39	68	47	48	59
Total # clones	96	82	94	69	90	81
Total nt sequenced	92,160	78,720	90,240	69,000	90,000	81,000
Mutations/10⁴ nt	11.07	4.95	7.53	6.81	5.56	7.28