

Supplementary Table S3a. Sequence and alignment statistics of each starting virus samples (including technical replicates).

	Sample	Replicate	Total reads	Mapped reads	Mean coverage	Frequency cut-off
Starting virus	Start 1	1	5.52x10 ⁵	97.83%	2.06x10 ⁴	0.20%
		2	6.35x10 ⁵	97.07%	2.35x10 ⁴	
	Start 2	1	2.42x10 ⁵	98.79%	8.44x10 ⁴	0.50%
		2	2.78x10 ⁵	98.57%	9.53x10 ⁴	
	Start 3	1	3.42x10 ⁵	99.10%	1.29x10 ⁴	0.50%
		2	3.61x10 ⁵	98.86%	1.36x10 ⁴	

Supplementary Table S3b. Sequence and alignment statistics of each sample (including technical replicates) within the Field group. Due to the low number of generated reads, sample Field-3817-P2 (highlighted in grey) was removed from downstream analysis.

	Sample	Passage	Replicate	Total reads	Mapped reads	Mean coverage	Frequency cut-off
Field	3159	1	1	4.58x10 ⁵	98.98%	1.75x10 ⁴	0.50%
			2	4.12x10 ⁵	98.74%	1.56x10 ⁴	
		2	1	4.60x10 ⁵	98.87%	1.74x10 ⁴	0.50%
			2	2.27x10 ⁵	97.86%	8.15x10 ³	
		3	1	2.86x10 ⁵	99.17%	1.08x10 ⁴	0.50%
			2	8.34x10 ⁵	99.05%	2.98x10 ³	
		4	1	3.28x10 ⁵	98.88%	1.25x10 ⁴	0.50%
			2	4.54x10 ⁵	98.87%	1.71x10 ⁴	
	3157	1	1	3.67x10 ⁵	93.38%	1.31x10 ⁴	0.20%
			2	1.20x10 ⁵	75.20%	3.28x10 ³	
		2	1	3.36x10 ⁵	95.10%	1.21x10 ⁴	0.20%
			2	3.34x10 ⁵	96.22%	1.21x10 ⁴	
	3817	1	1	1.98x10 ⁵	98.77%	6.99x10 ³	0.50%
			2	2.13x10 ⁵	98.87%	7.48x10 ³	
		2	1	2.25x10 ⁵	99.22%	7.96x10 ³	0.80%
			2	2.31x10 ³	3.45%	2.64x10 ⁰	
		3	1	1.92x10 ⁵	99.10%	6.87x10 ³	0.50%
			2	2.04x10 ⁵	99.29%	7.32x10 ³	
		4	1	2.74x10 ⁵	99.52%	9.83x10 ³	0.50%
			2	3.21x10 ⁵	99.47%	1.15x10 ⁴	

Supplementary Table S3c. Sequence and alignment statistics of each sample (including technical replicates) within Challenged group.

	Sample	Passage	Replicate	Total reads	Mapped reads	Mean coverage	Frequency cut-off
Challenged	4942	1	1	4.24x10 ⁵	98.44%	1.58x10 ⁴	0.50%
			2	3.75x10 ⁵	98.37%	1.39x10 ⁴	
		2	1	4.74x10 ⁵	98.94%	1.80x10 ⁴	0.50%
			2	3.85x10 ⁵	98.71%	1.41x10 ⁴	
		3	1	3.39x10 ⁵	98.73%	1.28x10 ⁴	0.50%
			2	5.52x10 ⁵	98.84%	2.08x10 ⁴	
		4	1	3.94x10 ⁵	98.63%	1.50x10 ⁴	0.50%
			2	4.11x10 ⁵	98.87%	1.57x10 ⁴	
	4926	1	1	5.12x10 ⁵	96.56%	1.88x10 ⁴	0.20%
			2	3.57x10 ⁵	96.20%	1.31x10 ⁴	
		2	1	5.35x10 ⁵	96.42%	1.98x10 ⁴	0.20%
			2	4.83x10 ⁵	95.36%	1.76x10 ⁴	
		3	1	4.45x10 ⁵	98.42%	1.67x10 ⁴	0.20%
			2	1.13x10 ⁵	97.49%	4.22x10 ⁴	
		4	1	3.29x10 ⁵	94.36%	1.17x10 ⁴	0.20%
			2	4.80x10 ⁵	96.61%	1.77x10 ⁴	
	4914	1	1	3.39x10 ⁵	99.22%	1.21x10 ⁴	0.50%
			2	2.40x10 ⁵	99.23%	8.47x10 ⁴	
		2	1	3.49x10 ⁵	99.38%	1.25x10 ⁴	0.50%
			2	3.56x10 ⁵	99.34%	1.27x10 ⁴	
		3	1	2.87x10 ⁵	99.00%	1.01x10 ⁴	0.50%
			2	2.49x10 ⁵	99.38%	8.88x10 ⁴	
		4	1	6.19x10 ⁵	99.16%	2.26x10 ⁴	0.50%
			2	5.51x10 ⁵	99.06%	2.02x10 ⁴	

Supplementary Table S3d. Sequence and alignment statistics of each sample (including technical replicates) within Control group.

	Sampl e	Passag e	Replicate	Total reads	Mapped reads	Mean coverage	Frequency cut-off
Control	4942C	1	1	3.01x10 ⁵	99.35%	1.17x10 ⁴	0.50%
			2	2.43x10 ⁵	99.34%	0.41x10 ³	
		2	1	2.80x10 ⁵	99.02%	1.08x10 ⁴	0.50%
			2	1.75x10 ⁵	99.49%	6.74x10 ³	
		3	1	5.24x10 ⁵	98.45%	1.98x10 ⁴	0.20%
			2	4.72x10 ⁵	98.46%	1.77x10 ⁴	
		4	1	3.89x10 ⁵	98.49%	1.44x10 ⁴	0.20%
			2	2.74x10 ⁵	98.48%	1.00x10 ⁴	
	4926C	1	1	5.91x10 ⁵	96.38%	2.19x10 ⁴	0.20%
			2	5.71x10 ⁵	95.91%	2.09x10 ⁴	
		2	1	4.39x10 ⁵	97.71%	1.64x10 ⁴	0.20%
			2	4.52x10 ⁵	98.46%	1.68x10 ⁴	
		3	1	3.70x10 ⁵	98.31%	1.39x10 ⁴	0.20%
			2	3.69x10 ⁵	97.88%	1.38x10 ⁴	
		4	1	5.60x10 ⁵	98.92%	2.13x10 ⁴	0.20%
			2	5.57x10 ⁵	98.60%	2.08x10 ⁴	
	4914C	1	1	3.24x10 ⁵	97.67%	1.10x10 ⁴	0.50%
			2	1.16x10 ⁵	98.63%	3.92x10 ³	
		2	1	2.46x10 ⁵	98.63%	8.46x10 ³	0.50%
			2	2.47x10 ⁵	98.06%	8.46x10 ³	
		3	1	3.25x10 ⁵	97.61%	1.09x10 ⁴	0.50%
			2	2.93x10 ⁵	98.36%	1.01x10 ⁴	
		4	1	2.28x10 ⁵	99.21%	8.20x10 ³	0.50%
			2	2.01x10 ⁵	98.72%	6.92x10 ³	