

Figure S1: Overview of the experimental procedures. Nucleotide sequences of the four types of viruses (dsDNA, dsRNA, ssRNA, and ssDNA) were extracted from viruSITE, and stringent BLASTn searches were conducted on a custom GenBank NR database. These sequences were then aligned, and these multiple sequence alignments (MSA) were subjected to two independent sets of analyses: one searching for evidence for adaptive (diversifying) selection based on the MEME algorithm, and another one searching for evidence for correlated evolution based on the SpiderMonkey algorithm.


Figure S2: Physical characteristics of the four types of viruses. Boxplots show the distribution of four features: (a) genome size, on a $\log _{10}$ scale; (b) number of genes; (c) number of proteins; (d) number of RNAs. These distributions are shown for dsDNA (blue), dsRNA (purple), ssDNA (orange), and ssRNA (red).


Figure S3: Viral diversity across viral types. Boxplots show the distribution of genetic diversity for each viral type, where diversity of each virus of each type is measured by computing the total tree length, divided by the number of sequences in each alignment. Similar results were obtained with mean patristic distances divided by number of sequences. Red bar indicate significant differences at the $1 \%$ false discovery rate level (Dunn test; Benjamini-Hochberg correction).

Table S1: GO enrichment tests for all the MEME genes of interests. Both tests are based on Fisher's exact test, either in its standard form ("classicFisher"), or in a version designed to be more conservative ("elimFisher"). $P<0.01$ in bold. Broad viral stages (GO.ID column): E: cell entry/exit; R: replication; T: transcription; A: assembly.

| VirTyp | GO | GO.ID | Term | Annotated | Significant | Expected | Rank in classicFisher | classicFisher | elimFisher |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| dsDNA | MF | GO:0004003 (R) | ATP-dependent DNA helicase activity | 122 | 70 | 20.94 | 1 | $1.80 \times 10^{-26}$ | $1.80 \times 10^{-26}$ |  |
|  |  | GO:0003677 (R) | DNA binding | 343 | 107 | 58.86 | 9 | $4.30 \times 10^{-14}$ | $4.30 \times 10^{-14}$ |  |
|  |  | GO:0003724 (R) | RNA helicase activity | 149 | 60 | 25.57 | 14 | $8.30 \times 10^{-13}$ | $8.30 \times 10^{-13}$ |  |
|  |  | GO:0005524 | ATP binding | 353 | 94 | 60.58 | 20 | $1.10 \times 10^{-7}$ | $1.10 \times 10^{-7}$ | 2 |
|  |  | GO:0003723 (R) | RNA binding | 262 | 64 | 44.96 | 32 | 0.00056 | 0.00056 |  |
|  |  | GO:0003700 (T) | DNA binding transcription factor activit... | 64 | 20 | 10.98 | 35 | 0.00338 | 0.00338 |  |
|  |  | GO:0019783 (R) | ubiquitin-like protein-specific protease... | 5 | 4 | 0.86 | 36 | 0.00367 | 0.00367 |  |
|  |  | GO:0005515 (E) | protein binding | 223 | 52 | 38.27 | 37 | 0.00635 | 0.00635 |  |
|  |  | GO:0016773 | phosphotransferase activity alcohol gro | 32 | 11 | 5.49 | 39 | 0.01332 | 0.01332 |  |
|  |  | GO:0005506 | iron ion binding | 10 | 5 | 1.72 | 40 | 0.01711 | 0.01711 |  |
|  | BP | GO:0006260 (R) | DNA replication | 184 | 84 | 24.83 | 1 | $<\mathbf{1} \times 10^{-30}$ | $5.30 \times 10^{-30}$ |  |
|  |  | GO:0019079 (R) | viral genome replication | 216 | 71 | 29.15 | 3 | $1.00 \times 10^{-16}$ | $1.00 \times 10^{-16}$ |  |
|  |  | GO:0006275 (R) | regulation of DNA replication | 25 | 11 | 3.37 | 28 | 0.00016 | 0.00016 |  |
|  |  | GO:0022900 | electron transport chain | 7 | 5 | 0.94 | 31 | 0.00071 | 0.00071 |  |
|  |  | GO:0040011 (E) | locomotion | 14 | 7 | 1.89 | 32 | 0.00108 | 0.00108 |  |
|  |  | GO:1901566 (R) | organonitrogen compound biosynthetic pro... | 37 | 11 | 4.99 | 34 | 0.00698 | 0.00698 |  |
|  |  | GO:0044283 (R) | small molecule biosynthetic process | 7 | 4 | 0.94 | 35 | 0.00806 | 0.00806 |  |
|  |  | GO:0006383 (T) | transcription from RNA polymerase III pr... | 4 | 3 | 0.54 | 36 | 0.00871 | 0.00871 |  |
|  |  | GO:0002252 | immune effector process | 2 | 2 | 0.27 | 38 | 0.01811 | 0.01811 |  |
|  |  | GO:0009072 | aromatic amino acid family metabolic pro... | 2 | 2 | 0.27 | 39 | 0.01811 | 0.01811 |  |
|  | CC | GO:0042025 (R) | host cell nucleus | 66 | 20 | 6.66 | 1 | $1.50 \times 10^{-6}$ | $1.50 \times 10^{-6}$ |  |
|  |  | GO:0005666 (T) | DNA-directed RNA polymerase III complex | 4 | 3 | 0.4 | 16 | 0.0037 | 0.0037 |  |
|  |  | GO:0005882 (R) | intermediate filament | 4 | 3 | 0.4 | 17 | 0.0037 | 0.0037 |  |
|  |  | GO:0033179 | proton-transporting V-type ATPase V0 do | 2 | 2 | 0.2 | 23 | 0.0101 | 0.0101 |  |
|  |  | GO:0045095 | keratin filament | 2 | 2 | 0.2 | 24 | 0.0101 | 0.0101 |  |
|  |  | GO:0046806 | viral scaffold | 2 | 2 | 0.2 | 25 | 0.0101 | 0.0101 |  |
|  |  | GO:0042597 | periplasmic space | 12 | 4 | 1.21 | 29 | 0.0255 | 0.0255 |  |
|  |  | GO:0005887 | integral component of plasma membrane | 3 | 2 | 0.3 | 31 | 0.0282 | 0.0282 |  |
|  |  | GO:0005929 | cilium | 3 | 2 | 0.3 | 32 | 0.0282 | 0.0282 |  |
|  |  | GO:0031226 | intrinsic component of plasma membrane | 3 | 2 | 0.3 | 33 | 0.0282 | 0.0282 |  |
| ssRNA | MF | GO:0003968 (R) | RNA-directed 5' ${ }^{\prime}$ ' RNA polymerase activi... | 257 | 84 | 28.5 | 1 | $3.90 \times 10^{-27}$ | $3.90 \times 10^{-27}$ |  |
|  |  | GO:0004197 (R) | cysteine-type endopeptidase activity | 52 | 28 | 5.77 | 10 | $8.00 \times 10^{-15}$ | $8.00 \times 10^{-15}$ |  |
|  |  | GO:0004252 (R) | serine-type endopeptidase activity | 79 | 29 | 8.76 | 18 | $4.90 \times 10^{-10}$ | $4.90 \times 10^{-10}$ |  |
|  |  | GO:0046983 (R) | protein dimerization activity | 38 | 18 | 4.21 | 20 | $1.20 \times 10^{-8}$ | $1.20 \times 10^{-8}$ |  |
|  |  | GO:0046789 (E) | host cell surface receptor binding | 31 | 16 | 3.44 | 21 | $1.70 \times 10^{-8}$ | $1.70 \times 10^{-8}$ |  |
|  |  | GO:0004482 (R) | mRNA (guanine-N7-)-methyltransferase act... | 86 | 26 | 9.54 | 25 | $4.50 \times 10^{-7}$ | $4.50 \times 10^{-7}$ |  |
|  |  | GO:0005198 (R) | structural molecule activity | 327 | 62 | 36.26 | 28 | $7.20 \times 10^{-7}$ | $7.20 \times 10^{-7}$ |  |
|  |  | GO:0003725 (R) | double-stranded RNA binding | 28 | 13 | 3.1 | 30 | $2.00 \times 10^{-6}$ | $2.00 \times 10^{-6}$ |  |
|  |  | GO:0004483 (R) | mRNA (nucleoside-2'-O-)-methyltransferas... | 27 | 12 | 2.99 | 32 | $\mathbf{9 . 1 0 \times 1 0 ^ { - 6 }}$ | $9.10 \times 10^{-6}$ | - |
|  |  | GO:0008168 (R) | methyltransferase activity | 113 | 37 | 12.53 | 16 | $6.30 \times 10^{-11}$ | $1.90 \times 10^{-5}$ | § |
|  | BP | GO:0006508 (R) | proteolysis | 120 | 49 | 15.71 | 2 | $4.40 \times 10^{-16}$ | $4.40 \times 10^{-19}$ |  |
|  |  | GO:0032259 (R) | methylation | 66 | 29 | 8.64 | 11 | $1.60 \times 10^{-10}$ | $1.60 \times 10^{-10}$ |  |
|  |  | GO:0019087 (R) | transformation of host cell by virus | 43 | 21 | 5.63 | 14 | $6.90 \times 10^{-9}$ | $6.90 \times 10^{-9}$ |  |
|  |  | GO:0019082 (R) | viral protein processing | 20 | 13 | 2.62 | 16 | $7.20 \times 10^{-8}$ | $7.20 \times 10^{-8}$ |  |
|  |  | GO:0019058 | viral life cycle | 411 | 87 | 53.81 | 13 | $6.70 \times 10^{-9}$ | $1.20 \times 10^{-5}$ |  |
|  |  | GO:0016070 | RNA metabolic process | 413 | 76 | 54.07 | 17 | $8.90 \times 10^{-5}$ | $8.90 \times 10^{-5}$ |  |
|  |  | GO:0019064 (E) | fusion of virus membrane with host plasm... | 48 | 16 | 6.28 | 18 | 0.00019 | 0.00019 |  |
|  |  | GO:0019048 | modulation by virus of host morphology o... | 84 | 39 | 11 | 3 | $5.10 \times 10^{-15}$ | 0.00021 |  |
|  |  | GO:0030683 | evasion or tolerance by virus of host im... | 24 | 10 | 3.14 | 29 | 0.00043 | 0.00043 |  |
|  |  | GO:0039694 (R) | viral RNA genome replication | 13 | 7 | 1.7 | 34 | 0.0005 | 0.0005 |  |
|  | CC | GO:0019031 | viral envelope | 164 | 51 | 25.27 | 2 | $9.60 \times 10^{-9}$ | $9.60 \times 10^{-9}$ |  |
|  |  | GO:0019012 | virion | 601 | 128 | 92.62 | 1 | $3.20 \times 10^{-14}$ | $3.00 \times 10^{-8}$ |  |
|  |  | GO:0055036 | virion membrane | 24 | 11 | 3.7 | 5 | 0.00033 | 0.00033 |  |
|  |  | GO:0044454 | nuclear chromosome part | 11 | 5 | 1.7 | 6 | 0.01712 | 0.01712 |  |
|  |  | GO:0000778 | condensed nuclear chromosome kinetochore | 10 | 4 | 1.54 | 7 | 0.05346 | 0.05346 |  |
|  |  | GO:0000780 | condensed nuclear chromosome centromeri | 10 | 4 | 1.54 | 8 | 0.05346 | 0.05346 |  |
|  |  | GO:0000942 | condensed nuclear chromosome outer kinet... | 10 | 4 | 1.54 | 9 | 0.05346 | 0.05346 |  |
|  |  | GO:0042729 | DASH complex | 10 | 4 | 1.54 | 10 | 0.05346 | 0.05346 |  |
|  |  | GO:0072686 | mitotic spindle | 10 | 4 | 1.54 | 11 | 0.05346 | 0.05346 |  |
|  |  | GO:0019030 | icosahedral viral capsid | 3 | 2 | 0.46 | 12 | 0.06362 | 0.06362 |  |

Table S2: GO enrichment tests for all the SM genes of interests. Both tests are based on Fisher's exact test, either in its standard form ("classicFisher"), or in a version designed to be more conservative ("elimFisher"). $P<0.01$ in bold. Broad viral stages (GO.ID column): E: cell entry/exit; R: replication; T: transcription; A: assembly.


Table S3: GO enrichment tests for all the SM+MEME genes of interests. Both tests are based on Fisher's exact test, either in its standard form ("classicFisher"), or in a version designed to be more conservative ("elimFisher"). $P<0.01$ $\underset{\text { VirTyp }}{\text { in bold. Broad viral stages (GO.ID column): E: cell entry/exit; R: replication; T: transcription; A: assembly. }}$

| VirTyp | GO | GO.ID | Term | Annotated | Significant | Expected | Rank in classicFisher | classicFisher | elimFisher |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| dsDNA | MF | GO:0005198 (R) | structural molecule activity | 327 | 9 | 2.54 | 1 | $6.00 \times 10^{-5}$ | $6.00 \times 10^{-5}$ |
|  |  | GO:0004252 | serine-type endopeptidase activity | 79 | 2 | 0.61 | 2 | 0.12 | 0.12 |
|  |  | GO:0008236 | serine-type peptidase activity | 90 | 2 | 0.7 | 3 | 0.15 | 0.15 |
|  |  | GO:0017171 | serine hydrolase activity | 90 | 2 | 0.7 | 4 | 0.15 | 0.15 |
|  |  | GO:0004175 | endopeptidase activity | 133 | 2 | 1.03 | 5 | 0.28 | 0.28 |
|  |  | GO:0070011 | peptidase activity acting on L-amino ac | 149 | 2 | 1.16 | 6 | 0.32 | 0.32 |
|  |  | GO:0008233 | peptidase activity | 153 | 2 | 1.19 | 7 | 0.34 | 0.34 |
|  |  | GO:0140096 | catalytic activity acting on a protein | 191 | 2 | 1.48 | 8 | 0.45 | 0.45 |
|  |  | GO:0003677 | DNA binding | 343 | 2 | 2.66 | 9 | 0.79 | 0.79 |
|  |  | GO:0016787 | hydrolase activity | 402 | 2 | 3.12 | 10 | 0.86 | 0.86 |
|  | BP | GO:0043158 | heterocyst differentiation | 6 | 2 | 0.02 | 1 | 0.00012 | 0.00012 |
|  |  | GO:0051726 | regulation of cell cycle | 7 | 2 | 0.02 | 2 | 0.00016 | 0.00016 |
|  |  | GO:0007049 | cell cycle | 29 | 2 | 0.09 | 6 | 0.00306 | 1 |
|  |  | GO:0008150 | biological_process | 1245 | 4 | 4 | 11 | 1 | 1 |
|  |  | GO:0009987 | cellular process | 809 | 4 | 2.6 | 10 | 0.17782 | 1 |
|  |  | GO:0030154 | cell differentiation | 15 | 2 | 0.05 | 3 | 0.0008 | 1 |
|  |  | GO:0032502 | developmental process | 20 | 2 | 0.06 | 5 | 0.00144 | 1 |
|  |  | GO:0048869 | cellular developmental process | 15 | 2 | 0.05 | 4 | 0.0008 | 1 |
|  |  | GO:0050789 | regulation of biological process | 225 | 2 | 0.72 | 8 | 0.15168 | 1 |
|  |  | GO:0050794 | regulation of cellular process | 206 | 2 | 0.66 | 7 | 0.12999 | 1 |
|  | CC | GO:0019028 (E) | viral capsid | 375 | 9 | 4.57 | 1 | 0.0077 | 0.0077 |
|  |  | GO:0005634 | nucleus | 49 | 2 | 0.6 | 3 | 0.1163 | 0.1163 |
|  |  | GO:0043231 | intracellular membrane-bounded organelle | 72 | 2 | 0.88 | 4 | 0.2169 | 0.2169 |
|  |  | GO:0043227 | membrane-bounded organelle | 80 | 2 | 0.98 | 6 | 0.2543 | 0.2543 |
|  |  | GO:0043229 | intracellular organelle | 101 | 2 | 1.23 | 7 | 0.3538 | 0.3538 |
|  |  | GO:0043226 | organelle | 110 | 2 | 1.34 | 8 | 0.3959 | 0.3959 |
|  |  | GO:0044424 | intracellular part | 136 | 2 | 1.66 | 9 | 0.5119 | 0.5119 |
|  |  | GO:0005622 | intracellular | 138 | 2 | 1.68 | 10 | 0.5203 | 0.5203 |
|  |  | GO:0005623 | cell | 171 | 2 | 2.09 | 11 | 0.6477 | 0.6477 |
|  |  | GO:0044464 | cell part | 171 | 2 | 2.09 | 12 | 0.6477 | 0.6477 |
| ssRNA | MF | GO:0046789 (E) | host cell surface receptor binding | 31 | 6 | 0.46 | 1 | $2.90 \times 10^{-6}$ | $2.90 \times 10^{-6}$ |
|  |  | GO:0005509 | calcium ion binding | 2 | 1 | 0.03 | 5 | 0.029 | 0.029 |
|  |  | GO:0005198 | structural molecule activity | 327 | 9 | 4.85 | ${ }_{6}$ | 0.034 | 0.034 |
|  |  | GO:0005200 | structural constituent of cytoskeleton | 3 | 1 | 0.04 | 7 | 0.044 | 0.044 |
|  |  | GO:0004483 | mRNA (nucleoside-2'-O-)-methyltransferas... | 27 | 2 | 0.4 | 8 | 0.059 | 0.059 |
|  |  | GO:0008171 | O-methyltransferase activity | 27 | 2 | 0.4 | 9 | 0.059 | 0.059 |
|  |  | GO:0070008 | serine-type exopeptidase activity | 27 | 2 | 0.4 | 10 | 0.059 | 0.059 |
|  |  | GO:0003725 | double-stranded RNA binding | 28 | 2 | 0.42 | 11 | 0.063 | 0.063 |
|  |  | GO:0003950 | NAD+ ADP-ribosyltransferase activity | 5 | 1 | 0.07 | 12 | 0.072 | 0.072 |
|  |  | GO:0016763 | transferase activity transferring pento | 5 | 1 | 0.07 | 13 | 0.072 | 0.072 |
|  | BP | GO:0006352 (T) | DNA-templated transcription initiation | 4 | 2 | 0.06 | 1 | 0.0013 | 0.0013 |
|  |  | GO:0019064 (E) | fusion of virus membrane with host plasm... | 48 | 4 | 0.73 | 3 | 0.0049 | 0.0049 |
|  |  | GO:0007155 | cell adhesion | 16 | 2 | 0.24 | 16 | 0.0233 | 0.0233 |
|  |  | GO:0006891 | intra-Golgi vesicle-mediated transport | 3 | 1 | 0.05 | 17 | 0.0451 | 0.0451 |
|  |  | GO:0019058 | viral life cycle | 411 | 12 | 6.27 | 13 | 0.0064 | 0.052 |
|  |  | GO:0022610 | biological adhesion | 27 | 2 | 0.41 | 22 | 0.0617 | 0.0617 |
|  |  | GO:0006471 | protein ADP-ribosylation | 5 | 1 | 0.08 | 24 | 0.0741 | 0.0741 |
|  |  | GO:0006486 | protein glycosylation | 5 | 1 | 0.08 | 25 | 0.0741 | 0.0741 |
|  |  | GO:0009100 | glycoprotein metabolic process | 5 | 1 | 0.08 | 26 | 0.0741 | 0.0741 |
|  |  | GO:0009101 | glycoprotein biosynthetic process | 5 | 1 | 0.08 | 27 | 0.0741 | 0.0741 |
|  | CC | GO:0019031 (E) | viral envelope | 164 | 12 | 4.36 | 1 | 0.00032 | 0.00032 |
|  |  | GO:0009654 | photosystem II oxygen evolving complex | 1 | 1 | 0.03 | 3 | 0.02661 | 0.02661 |
|  |  | GO:0019898 | extrinsic component of membrane | 1 | 1 | 0.03 | 4 | 0.02661 | 0.02661 |
|  |  | GO:1990204 | oxidoreductase complex | 1 | 1 | 0.03 | 5 | 0.02661 | 0.02661 |
|  |  | GO:0043234 | protein complex | 72 | 5 | 1.92 | 6 | 0.03611 | 0.03611 |
|  |  | GO:0033180 | proton-transporting V-type ATPase V1 do | 2 | 1 | 0.05 | 7 | 0.05254 | 0.05254 |
|  |  | GO:0009521 | photosystem | 3 | 1 | 0.08 | 8 | 0.0778 | 0.0778 |
|  |  | GO:0009523 | photosystem II | 3 | 1 | 0.08 | 9 | 0.0778 | 0.0778 |
|  |  | GO:0017119 | Golgi transport complex | 3 | 1 | 0.08 | 10 | 0.0778 | 0.0778 |
|  |  | GO:0044431 | Golgi apparatus part | 3 | 1 | 0.08 | 11 | 0.0778 | 0.0778 |

