Electronic Supplementary Material (ESI) for Nanoscale.

SUPPLEMENTARY INFORMATION

Mechanical stiffening of human rhinovirus by cavity-filling antiviral drugs

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Table S1. Statistical significance of differences between average k_e values for HRV14 and mutants[a]

	WT	WT+piro	WT+pleco	V1188L	V1188A	C1199Y	Y1152W
WT	-	$6\cdot10^{-9}$	$2\cdot10^{-7}$	0.78	0.89	0.06	$3\cdot10^{-8}$
WT+piro		-	0.86	$2\cdot10^{-8}$	$2\cdot10^{-3}$	10^{-5}	0.65
WT+pleco			-	$4\cdot10^{-7}$	$3\cdot10^{-3}$	$9\cdot10^{-5}$	0.81
V1188L				-	0.80	0.10	$6\cdot10^{-8}$
V1188A					-	0.34	$4\cdot10^{-3}$
C1199Y						-	$4\cdot10^{-5}$
Y1152W							-

[a] p values obtained in Student's t tests are indicated. Values below 0.05 are considered as significantly different. WT, drug-free nonmutated HRV14; WT+piro, WT+pleco, WT incubated with 0.5 μM pirodavir or pleconaril, respectively.

Table S2. Statistical significance of differences between k_e values for different regions (S2, S3, S5) in HRV14 and mutants[a]

	S2-S3	S2-S5	S3-S5
WT	0.27	0.35	0.73
WT+piro	0.71	$2\cdot10^{-5}$	$2\cdot10^{-3}$
WT+pleco	0.16	$8\cdot10^{-5}$	$3\cdot10^{-3}$
V1188L	0.03	0.59	0.13
C1199Y	0.09	0.79	0.05
Y1152W	0.33	0.49	0.33

[a] p values obtained in Student's t tests are indicated. Values below 0.05 are considered as significantly different. WT, drug-free, nonmutated HRV14; WT+piro, WT+pleco, WT incubated with 0.5 μM pirodavir or pleconaril, respectively.

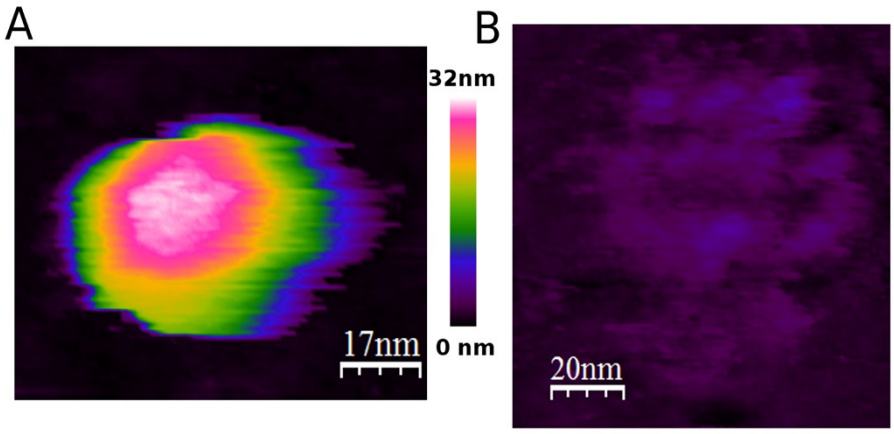

Figure S1. Mechanical disruption of HRV14 particles. (A) close-up of a HRV14 virion visualized by scanning a ~200 nm x ~200 nm field. (B) the same particle collapsed into small fragments when the scanning field size was decreased (to < 100 nm x 100 nm) as a prerequisite to perform indentations for stiffness analysis. Height at each image point in the image is color-coded as indicated in the calibrated scale between images. Horizontal scale bars are included.

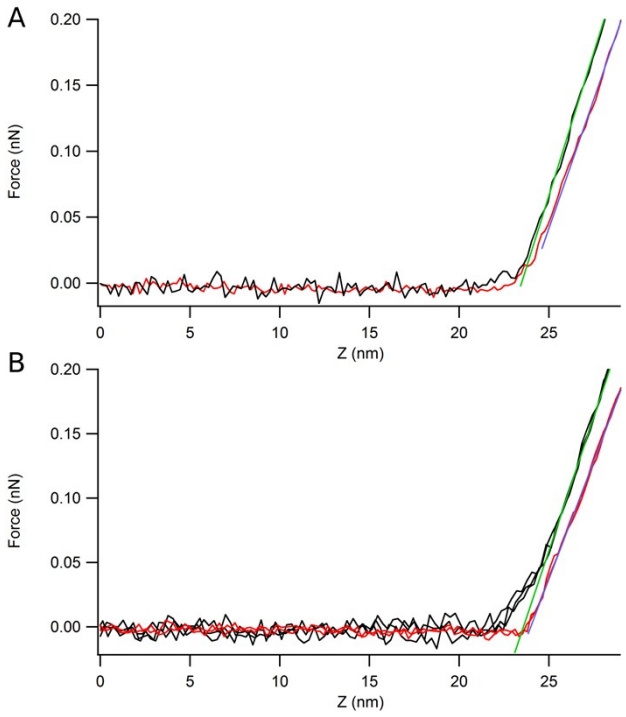

Figure S2. Representative *F-Z* curves. A, B, correspond to indentations using two different virions in different experiments. Plots of force *versus* piezo displacement correspond either to indentation on the substrate (black traces) or on a virion (red traces). The regions corresponding to the elastic regime are fitted to straight lines (green or blue for indentations on the substrate or the virion, respectively). Regression values: A, R=0.9996 (substrate), R=0.9980 (virion). B, R=0.9997 (substrate), R=0.9965 (virion).

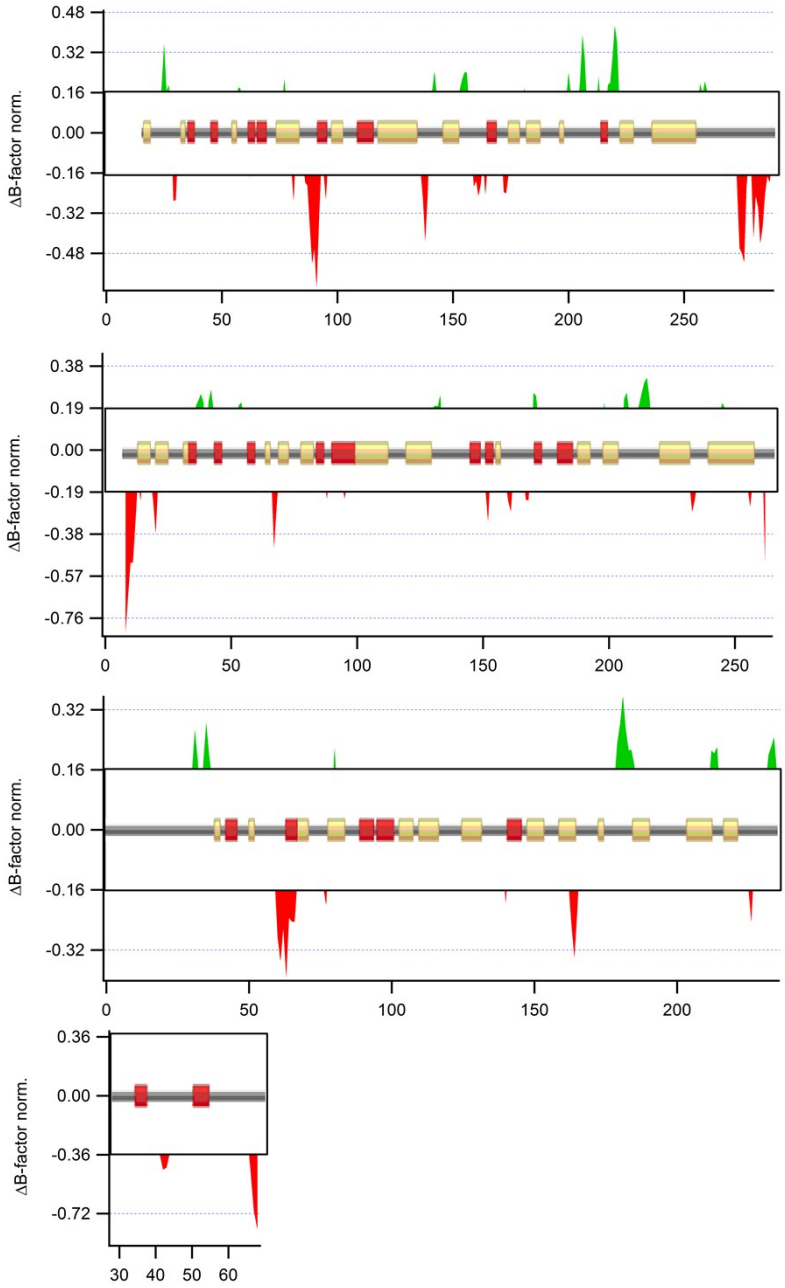

Figure S3. Differences between normalized B-factors (ΔB-factor$_{norm}$) for each Cα atom in the X-ray structures of the HRV14 virion without (PDB: 4RHV) or with (PDB: 1NA1) bound pleconaril. Normalized B-factors (B_{norm}) for each Cα atom were obtained by dividing each individual B-factor by the average B-factor for all Cα atoms in the same crystallographic model. ΔB-factor$_{norm}$ was obtained by substracting B_{norm} in the absence of drug from B_{norm} in the presence of drug. Only values larger than the standard deviation are indicated. Positive (green) or negative (red) ΔB-factor$_{norm}$ values correspond to Cαs whose B_{norm} respectively increased or decreased in the presence of drug. Secondary structure elements of each capsid protein (VP1-4) are indicated (red boxes: α-helices; yellow boxes: β-strands; gray line: loops and terminal segments). Top to bottom plots refer to VP1, VP2, VP3 and VP4.

Video S1. A comparison between the X-ray structures of HRV14 either without or with bound pleconaril. Views of the HRV14 biological protomer without pleconaril (PDB ID: 4RHV)[38] ("No Drug") or with bound pleconaril (PDB ID: 1NA1)[55] ("Bound Drug") are alternatively presented. The pleconaril molecule is depicted as a yellow spacefilling model. Regions that include residues whose Cα atoms show either higher or lower B_{norm} values when the drug is bound are colored green or red, respectively. Residues that line the pocket and that substantially change their mobility upon drug binding are represented as red (lower mobility) or green (higher mobility) spacefilling models.