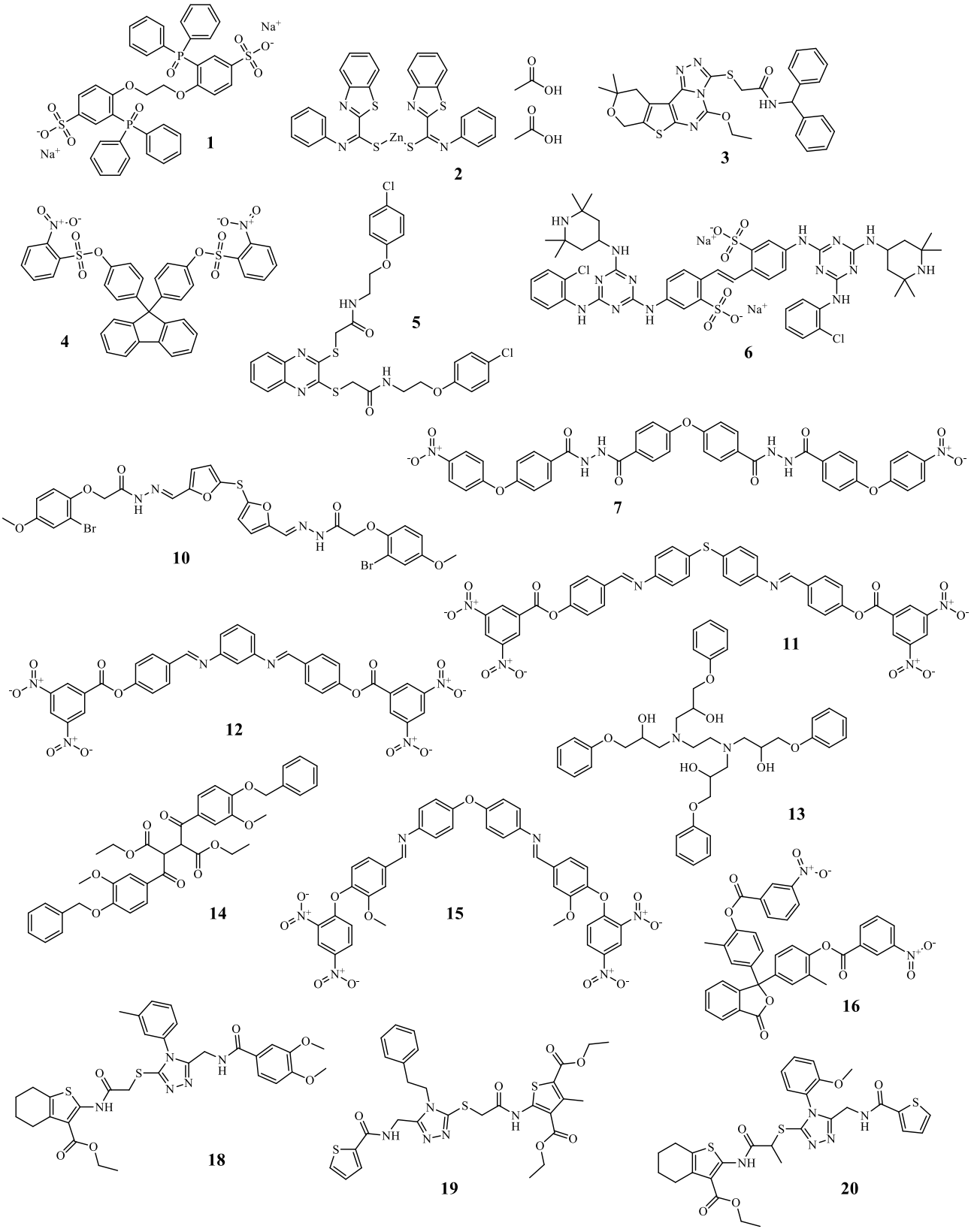
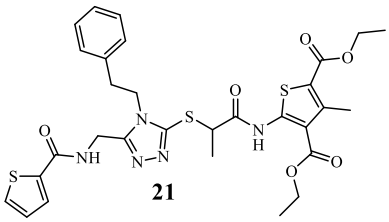
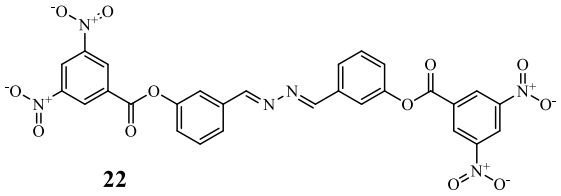
Appendix

**Appendix Figure S1:** Chemical structures of the initial compounds assayed in **Fig. 1A** (compounds **1**-**40**).





21



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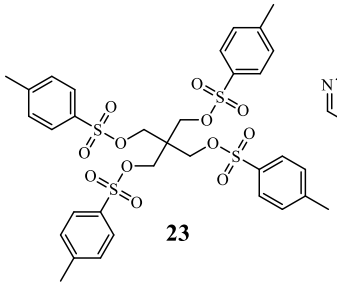
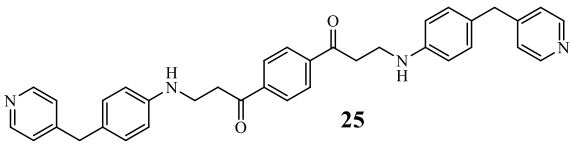


23



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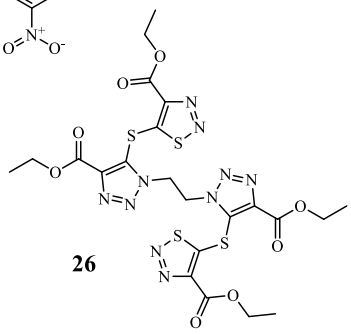

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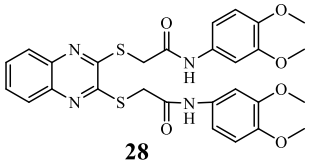

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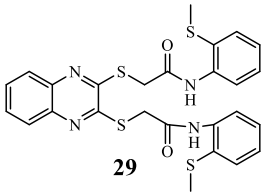

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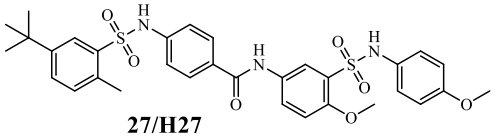
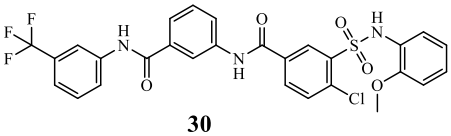


27/H27



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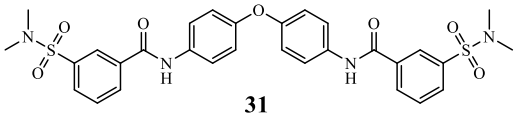

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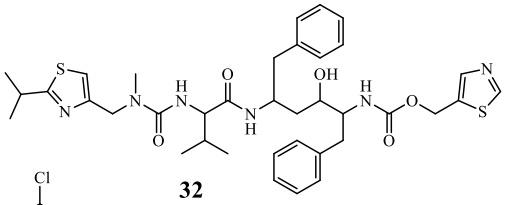

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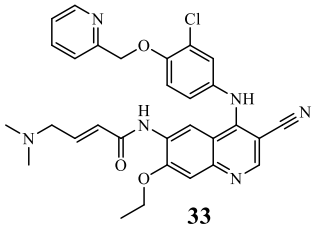

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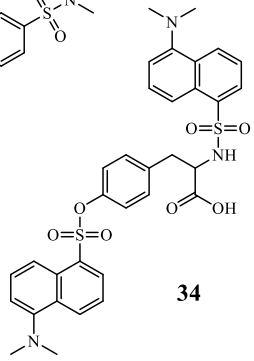

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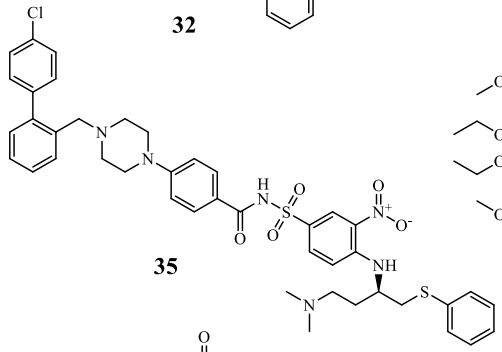

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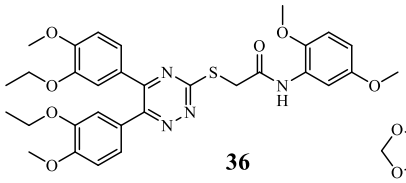

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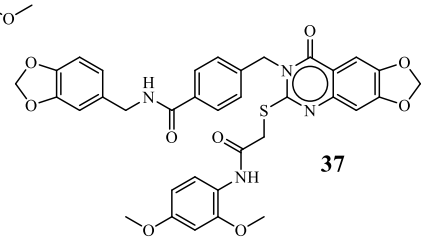
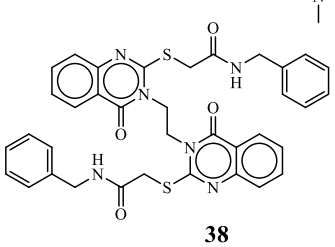


37



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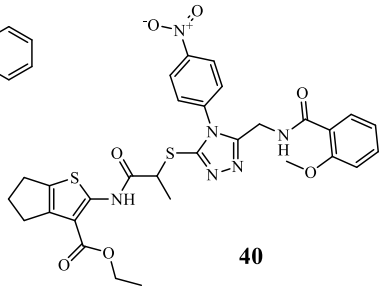

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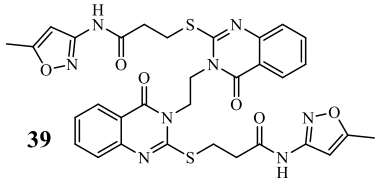
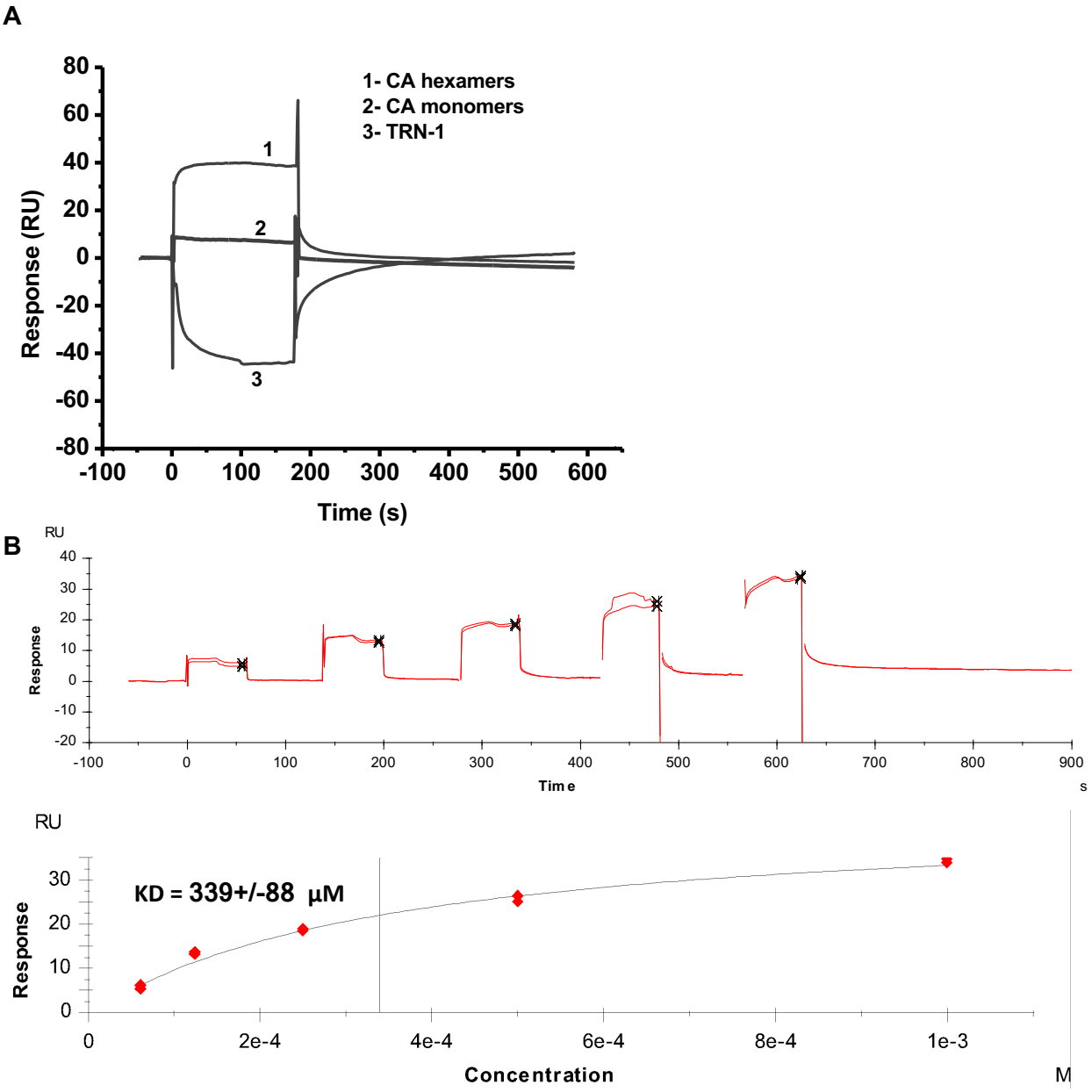
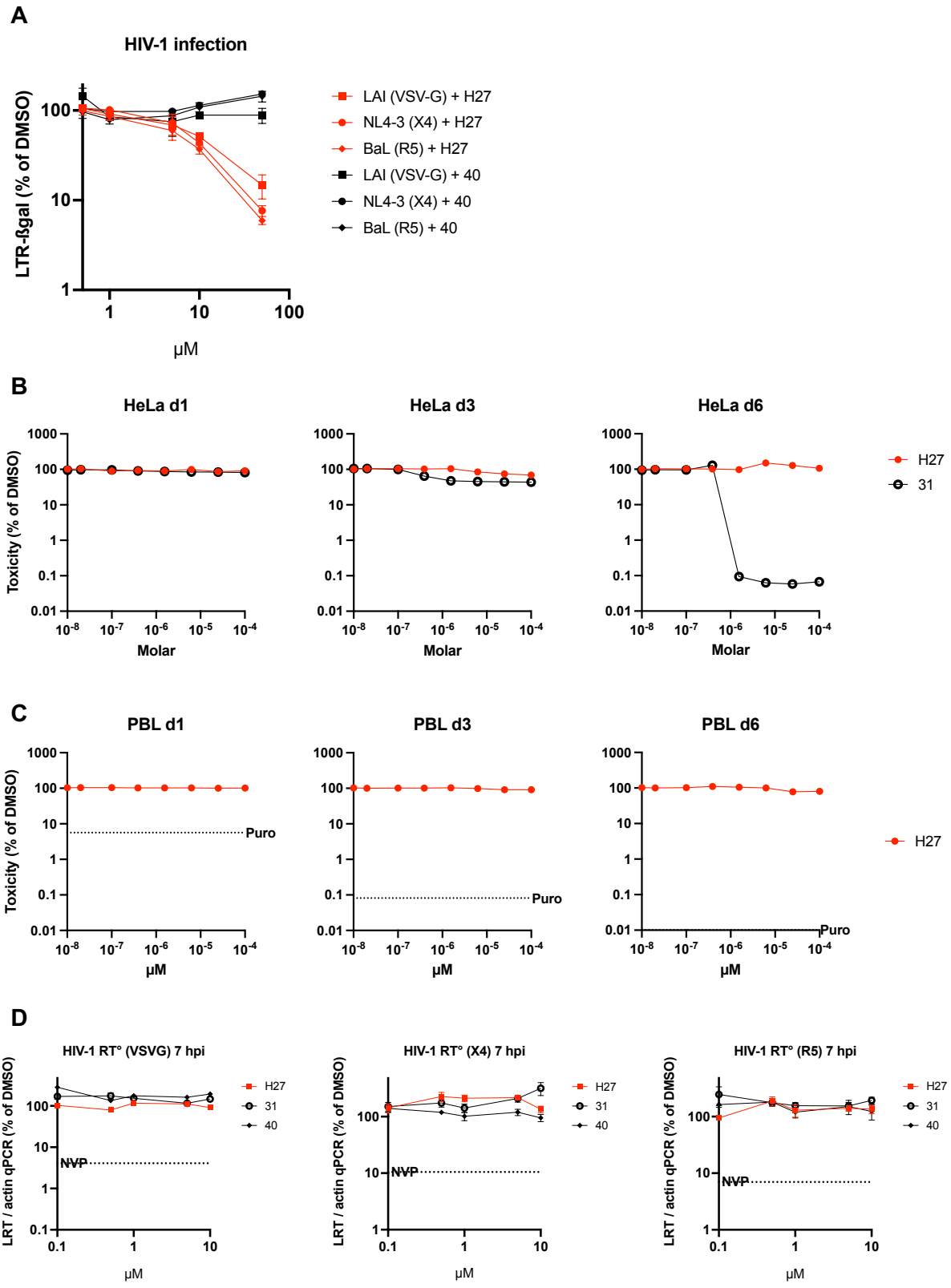


39

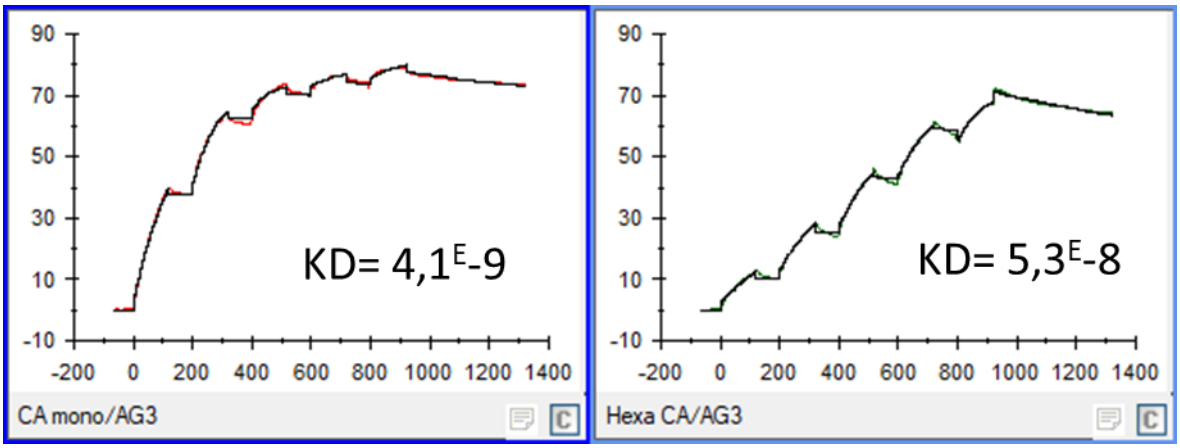
**Appendix Figure S2: Binding affinity of H27 to HIV-1 hexamers. (A)** SPR analysis of H27 (500 µM) binding to HIV-1 CA monomers (48,00RU), hexamers (14,000 RU, and to TRN-1 (14,000 RU) immobilized on a CM-5 sensor chip. **(B)** Determination of $K_D$ of H27 for immobilized HIV-1 CA hexamers by one cycle kinetic titration at five increasing H27 concentrations (62, 125, 250, 500 and 1,000 µM).



**Appendix Figure S3: Effect of H27 on infection, cell viability and HIV-1 reverse transcription. (A)** All tested HIV-1 were equally sensitive to H27, regardless of the tropism of their envelope. Infectivity in HeLa-R5 cells was assessed by ß-gal chemiluminescent assay at 48 hpi. Results show mean triplicate values ± SD from 2 independent experiments. For toxicity kinetics in **(B)** HeLa-R5 cells and **(C)** peripheral blood lymphocytes (PBL), cells were treated with H27 and compound **31** at concentrations ranging between 0.01 and 100 µM for 1, 3 or 6 days. Toxicity was assessed by Cell Titer assay. Results are representative of 2 independent experiments. Puromycin (2 µg/mL) was added to PBL as positive control. **(D)** Effect of H27 on reverse transcription at 7 hpi. HeLa-R5 cells were pre-treated with compounds at the indicated concentrations, then infected with VSV-G pseudotyped LAI, X4 tropic NL4-3 or R5-tropic BaL virus, at 1 ng p24/1,000 cells for 7 h. Compounds **31** and **40** were included as negative controls since they do not affect HIV-1 infection. Results are the mean of 2 independent experiments ± SEM normalised for the corresponding DMSO control. The reverse transcriptase inhibitor NVP (5 µM) were included as a negative control in all experiments. Reverse transcription (RT°) efficiency was assessed by qPCR amplification of late reverse transcripts (LRT) and normalised for Actin values.

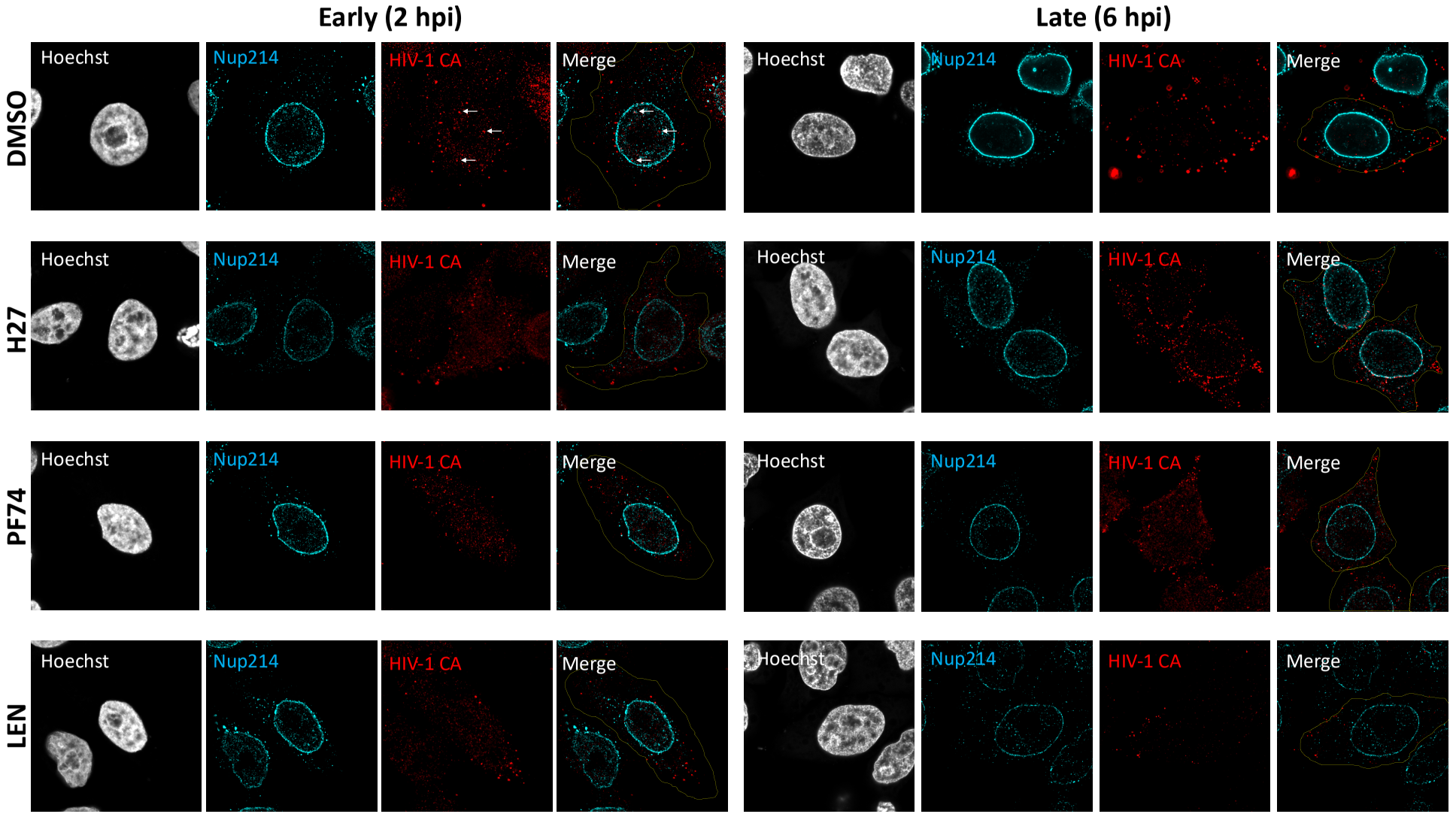

A
HIV-1 infection
LTR-βgal (% of DMSO)
100
10
1
1
10
100
µM
LAI (VSV-G) + H27
NL4-3 (X4) + H27
BaL (R5) + H27
LAI (VSV-G) + 40
NL4-3 (X4) + 40
BaL (R5) + 40
B
HeLa d1
HeLa d3
HeLa d6
Toxicity (% of DMSO)
1000
100
10
1
0.1
0.01
10-8 10-7 10-6 10-5 10-4
Molar
H27
31
C
PBL d1
PBL d3
PBL d6
Toxicity (% of DMSO)
Puro
µM
H27
D
HIV-1 RT° (VSVG) 7 hpi
HIV-1 RT° (X4) 7 hpi
HIV-1 RT° (R5) 7 hpi
LRT / actin qPCR (% of DMSO)
NVP
0.1
1
10
µM
H27
31
40

**Appendix Figure S4: SPR measurement of AG3.0 antibody kinetics against monomeric and hexameric capsids.** The affinity of AG3.0 antibody against monomeric and hexameric capsids were performed using one cycle kinetic titration by capture of AG3.0 (220 RU) on immobilized mouse anti-Fc and injecting monomeric CA from 10 to 160 nM and hexameric CA from 100 to 1600 nM, as two-fold dilution series. The $K_D$ were calculated using a bivalent fitting model.

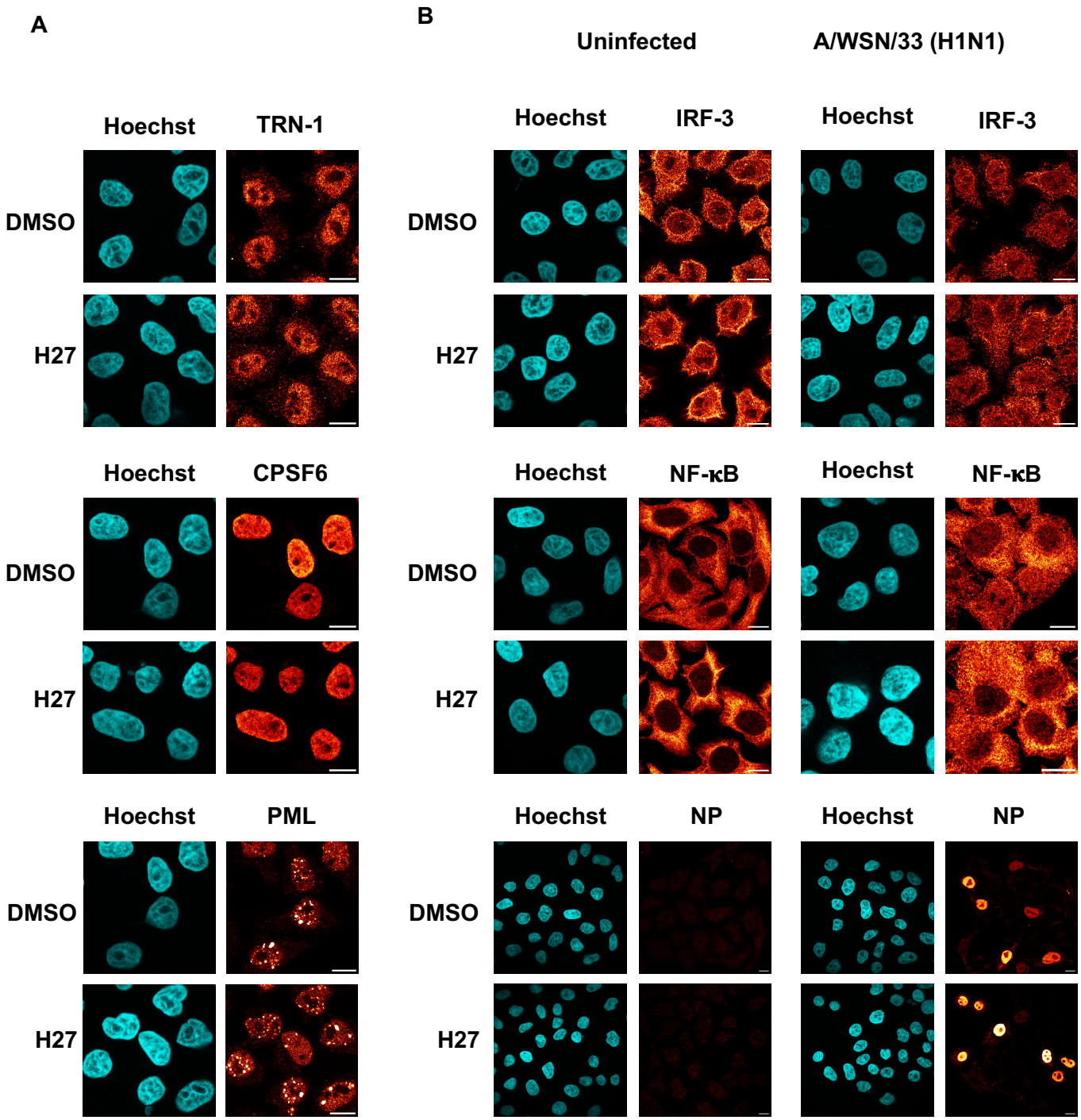



| Sample | ka (1/Ms) | kd (1/s) | **KD(M)** | Chi² (RU²) |
|---|---|---|---|---|
| CA mono | 1,69E+05 | 6,96E-04 | **4,12E-09** | 0,426 |
| Hexa CA | 5,93E+03 | 3,20E-04 | **5,39E-08** | 0,478 |

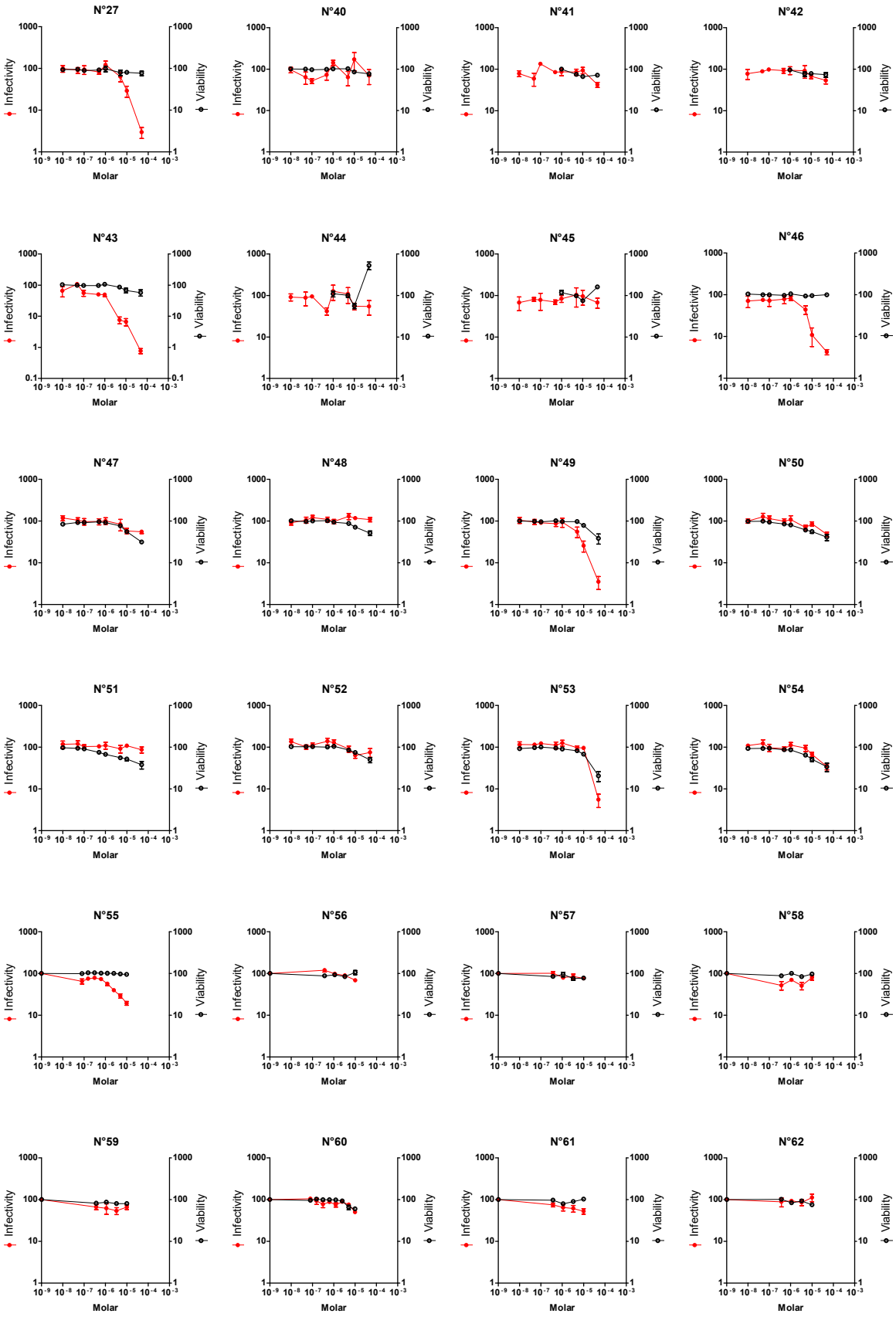
**Appendix Figure S5: CA localisation following treatment with H27, PF74 or LEN.** HeLa-R5 were treated with H27 (3 μM), PF74 (1 μM), LEN (9 nM), or DMSO (0.5%), then inoculated with LAI-VSV-G at 1 ng p24/1,000 cells in serum-free medium to promote cell attachment, then incubated in 10% FCS for a further 2 h or 6 h to allow infection to proceed. Samples were fixed, permeabilised and labelled with anti-CA and -Nup214 antibodies, and stained with Hoechst. Images were acquired on a LSM880 Airyscan confocal microscope with a 63 × objective. The cell periphery was delineated using the line tool from FiJi using cell autofluorescence. Arrows point to intranuclear CA spots. Images are representative of 3 independent experiments.

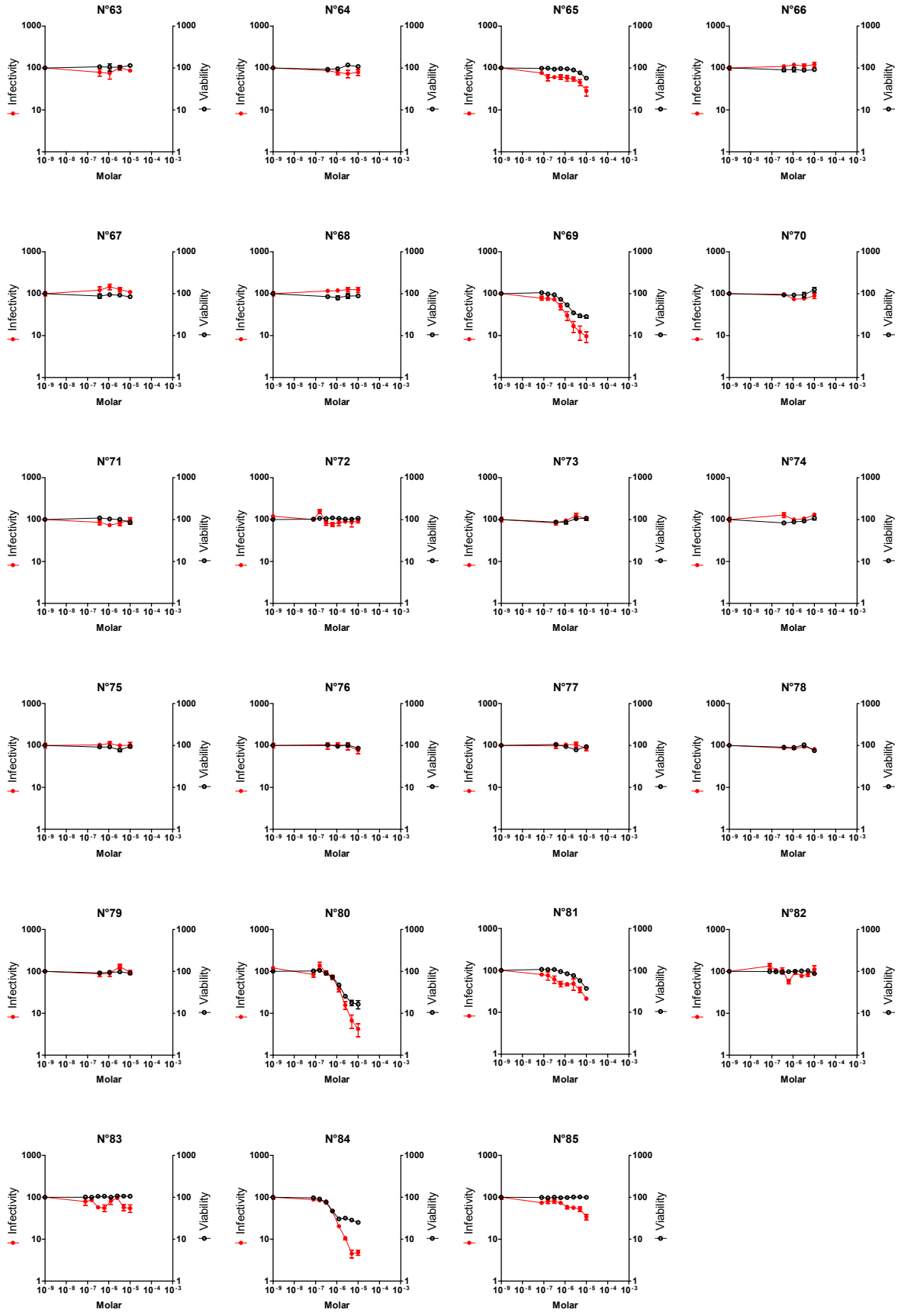

Early (2 hpi)
Late (6 hpi)
DMSO
H27
PF74
LEN
Hoechst
Nup214
HIV-1 CA
Merge

**Appendix Figure S6: Effect of H27 on the subcellular localization of shuttling proteins.** **(A)** HeLa-R5 cells were treated with DMSO or H27 (10 µM) for 8 h, then fixed and labelled with antibodies recognizing the shuttling proteins TRN-1, CPSF6 and PML. **(B)** HeLa-R5 cells were pre-treated with DMSO or H27 (10 µM) for 2 h, then stimulated with Influenza A virus (WSN strain) at 0.1 TCID50/cell. Cells were fixed after 6 h and labelled with antibodies recognizing the innate immune transcription factors IRF-3 and NF-$\kappa$B or the viral nucleoprotein (NP). Scale bars = 10 µm.



**Appendix Figure S7: Infectivity and toxicity of H27 and analogues 41 - 85.** The infectivity and toxicity of H27 and its structural analogues (compounds **41** to **85**) were assessed in HeLa-R5 cells. Infectivity was determined at 48 hpi following infection with HIV-1-VSV-G at 0.1 ng p24/1,000 cells, and toxicity was assessed in separate plates by Cell Titer assay in HeLa-R5 cells. Results show the mean ± SD of 2 independent experiments performed in triplicate.


N°27
N°40
N°41
N°42
N°43
N°44
N°45
N°46
N°47
N°48
N°49
N°50
N°51
N°52
N°53
N°54
N°55
N°56
N°57
N°58
N°59
N°60
N°61
N°62
Infectivity
Viability
Molar


N°63
N°64
N°65
N°66
N°67
N°68
N°69
N°70
N°71
N°72
N°73
N°74
N°75
N°76
N°77
N°78
N°79
N°80
N°81
N°82
N°83
N°84
N°85
Infectivity
Viability
Molar

**Appendix Figure S8: Sequence alignments of primate lentiviral CA.** Alignment of the capsid of HIV-1M and SIVgsn-99CM71, SIVmon-99CMCML1, SIVagmSAB, SIVmac251, HIV-$2_{ROD}$, SIVmnd2 and SIVcolCGU1. Dots represent fully conserved residues and deletions are indicated with dashes. The PY-NLS recognised by TRN-1 is highlighted in yellow.

```
                  10        20        30        40        50        60        70        80        90
                   |         |         |         |         |         |         |         |         |
HIV-1M       PIVQNLQGQMVHQAISPRTLNAWVKVIEEKAFSPEVIPMFSALSEGATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEWDRLHPVHAGPIAPGQM
SIVgsn       ...R.A...FQ...LNS.V.KT..SIV...K.A..TVAL.Q..T..CI.Y.M.Q...A..DY.G.V.II.DV...Q.....L...QP.A.QPVAGI
SIVmon       .V.RTQG.GFQ...VE..L.KT..Q.....K.A...VAL.Q.....MI.Y.I.QL..AI.D..G.L.II.DV......N..LV..QPPQ.QPNAGI
SIVagmSAB    .-IVSVNN.W...PL..............K..A..V......A...I.Y.I.Q...A..E..G.L.IV.DV......D..LR..PPQQ.P.Q.VI
SIVmac251    .-..QIG.NY..LPL..........L....K.GA..V.G.Q.....C..Y.I.Q...C..D......IIRDI......D..LQ..QP.-.Q-Q..I
HIV2ROD      .-..HVG.NYT.IPL..........LV...K.GA..V.G.Q.....C..Y.I.Q...C..D......IIR.I.........VQ..IPG-.LPA..I
SIVmnd2      .-I.VINQTP...G...........C....K....IV...I.....CI.Y...G...AI.D..G.L.IV.DV......D..LR..PVG-.MPQ.VI
SIVcol       ...TGP..-P...PL.....G....CV.G-GIA.SLA...L.Y.T..IAY.M.L...ILDT..GFP.V..DE..KK.E.Y.L....QQ-.QQQ.AI

                 110       120       130       140       150       160       170       180       190
                   |         |         |         |         |         |         |         |         |
HIV-1M       GSDIAGTTSTLQEQIGWMTN-NPPIPVGEIYKRWIILGLNKIVRMYSPVSILDIRQGPKEPFRDYVDRFYKTLRAEQATQEVKNWMTETLLVQNAN
SIVgsn       .A....V...PN...E.I.RQ.N.VN.AD..RK......QRC.K..N..N..G.K.......KE.....F.C......D.A......QL.......
SIVmon       .A....VS..P.Q..E.I.RA.N.VQ.SD..RK.V....QRC.K..N..N....K.......K........C.....TD.A......Q........
SIVagmSAB    ..........I....E.T.RAQNAVN..N...G......Q.C.K..N..N....K.......K........A.....TDPA......QS..I.....
SIVmac251    .........SVD...Q..YRQQN.....N..R...Q...Q.C....N.TN...VK.......QS.......S.....TDAA......Q...I.....
HIV2ROD      ..........VE...Q..FRPQN.V...N..R...QI..Q.C....N.TN....K.......QS.......S.....TDPA......Q........
SIVmnd2      .N.......SIE...E.T.RQQDQVN..G...Q..V...Q.C.S..N..N....K.......K........A....RTDPQ..T...Q...I.....
SIVcol       A...T.N..SVA..VA.GEP------IAN..RG..VQS.E.VIQIAR.S.V......S..D.KS......SA....P.AG.I.A..ANN..I.H..

                210       220       230
                 |         |         |
HIV-1M       TILKALGPAATLEEMMTACQGVGGPGHKARV
SIVgsn       L....MPG-.S....L.........T..S.L
SIVmon       L....MPG-.S..D.LQ........M..S.I
SIVagmSAB    .V..G..MNP.....L.....I..AQ....L
SIVmac251    LV..G..VNP.....L..........Q...L
HIV2ROD      LV..G..MNP.....L..........Q...L
SIVmnd2      AT..G..MNP.....LL........KY..QM
SIVcol       RI..G.QK-PS..D.LA........D...K.
```

**Appendix Figure S9: Listing of CA residues from two adjacent monomers within a hexamer that contact H27.** Residues either from **(A)** HIV-1 or from **(B)** SIVmac in contact with H27 (ranked by contact frequency during MD simulations showing only high frequency contact (> 10%)). Sustained binding observed with residues belonging to the PR loop are highlighted in yellow and common residues between HIV-1 and SIVmac CA are underlined in grey. **(C)** PY-NLS that is recognized by TRN-1, and corresponding residues for SIVmac251. Residues implicated in sustained contact with H27 are highlighted in yellow.

**A**

| Ligand | ResName | Monomer | ResNumber | Contact (%) |
|---|---|---|---|---|
| H27 | PRO | A | 125 | 59.3 |
| H27 | PRO | A | 122 | 57.3 |
| H27 | MET | A | 96 | 52 |
| H27 | PRO | A | 123 | 51.1 |
| H27 | GLN | B | 112 | 46.4 |
| H27 | GLN | A | 4 | 45.8 |
| H27 | THR | B | 110 | 44.6 |
| H27 | ILE | B | 115 | 44.3 |
| H27 | ILE | A | 124 | 41.9 |
| H27 | GLY | B | 116 | 40.6 |
| H27 | ILE | A | 129 | 39.7 |
| H27 | TRP | A | 80 | 39.4 |
| H27 | PRO | B | 93 | 37.3 |
| H27 | ARG | A | 132 | 36.1 |
| H27 | THR | B | 119 | 36 |
| H27 | GLY | B | 94 | 35.9 |
| H27 | GLN | B | 95 | 34.8 |
| H27 | LEU | A | 6 | 34.1 |
| H27 | HIS | B | 12 | 33.2 |
| H27 | GLU | B | 113 | 31.7 |
| H27 | HIS | A | 84 | 30.4 |
| H27 | VAL | B | 11 | 30.1 |
| H27 | MET | A | 10 | 29.6 |
| H27 | HIS | A | 120 | 29.1 |
| H27 | PRO | A | 99 | 28.5 |
| H27 | ASN | A | 5 | 28 |
| H27 | HIS | B | 120 | 27.9 |
| H27 | MET | B | 10 | 25.2 |
| H27 | LEU | A | 83 | 24.7 |
| H27 | TRP | B | 117 | 24.2 |
| H27 | ALA | B | 92 | 23.3 |
| H27 | GLN | B | 9 | 20.8 |
| H27 | GLU | A | 98 | 20.5 |
| H27 | GLU | A | 128 | 19.6 |
| H27 | MET | A | 118 | 18.7 |
| H27 | GLU | A | 79 | 16.7 |
| H27 | ILE | B | 124 | 16.4 |
| H27 | TRP | A | 133 | 15.7 |
| H27 | ASN | A | 121 | 15.4 |
| H27 | ARG | B | 97 | 13.7 |
| H27 | GLN | A | 9 | 13 |
| H27 | ILE | A | 2 | 10 |

**B**

| Ligand | ResName | Monomer | ResNumber | Contact (%) |
|---|---|---|---|---|
| H27 | VAL | B | 10 | 96.4 |
| H27 | TYR | A | 9 | 92.7 |
| H27 | ASP | B | 109 | 92.2 |
| H27 | TYR | A | 116 | 88.7 |
| H27 | GLN | A | 118 | 88.4 |
| H27 | HIS | B | 11 | 84.9 |
| H27 | VAL | B | 108 | 84.7 |
| H27 | PRO | A | 121 | 81.1 |
| H27 | ILE | B | 112 | 78.9 |
| H27 | ARG | A | 117 | 67.6 |
| H27 | ILE | B | 5 | 62.4 |
| H27 | VAL | A | 2 | 60.2 |
| H27 | GLN | A | 113 | 52 |
| H27 | GLN | A | 4 | 51.3 |
| H27 | ILE | A | 112 | 51.1 |
| H27 | PRO | A | 123 | 43.1 |
| H27 | TYR | B | 9 | 42.4 |
| H27 | GLN | B | 3 | 35.8 |
| H27 | PRO | B | 13 | 34.4 |
| H27 | HIS | A | 11 | 33.6 |
| H27 | GLY | A | 7 | 31.1 |
| H27 | TYR | B | 49 | 30.9 |
| H27 | LEU | B | 12 | 30 |
| H27 | ASN | B | 8 | 29.3 |
| H27 | VAL | A | 10 | 28.2 |
| H27 | GLN | B | 113 | 24.7 |
| H27 | MET | A | 115 | 23.6 |
| H27 | ASN | A | 8 | 21.6 |
| H27 | VAL | B | 2 | 17.8 |
| H27 | GLN | A | 3 | 14.9 |
| H27 | GLY | B | 6 | 13.8 |
| H27 | ASN | A | 120 | 10.7 |
| H27 | ASN | A | 126 | 10.2 |

**C**

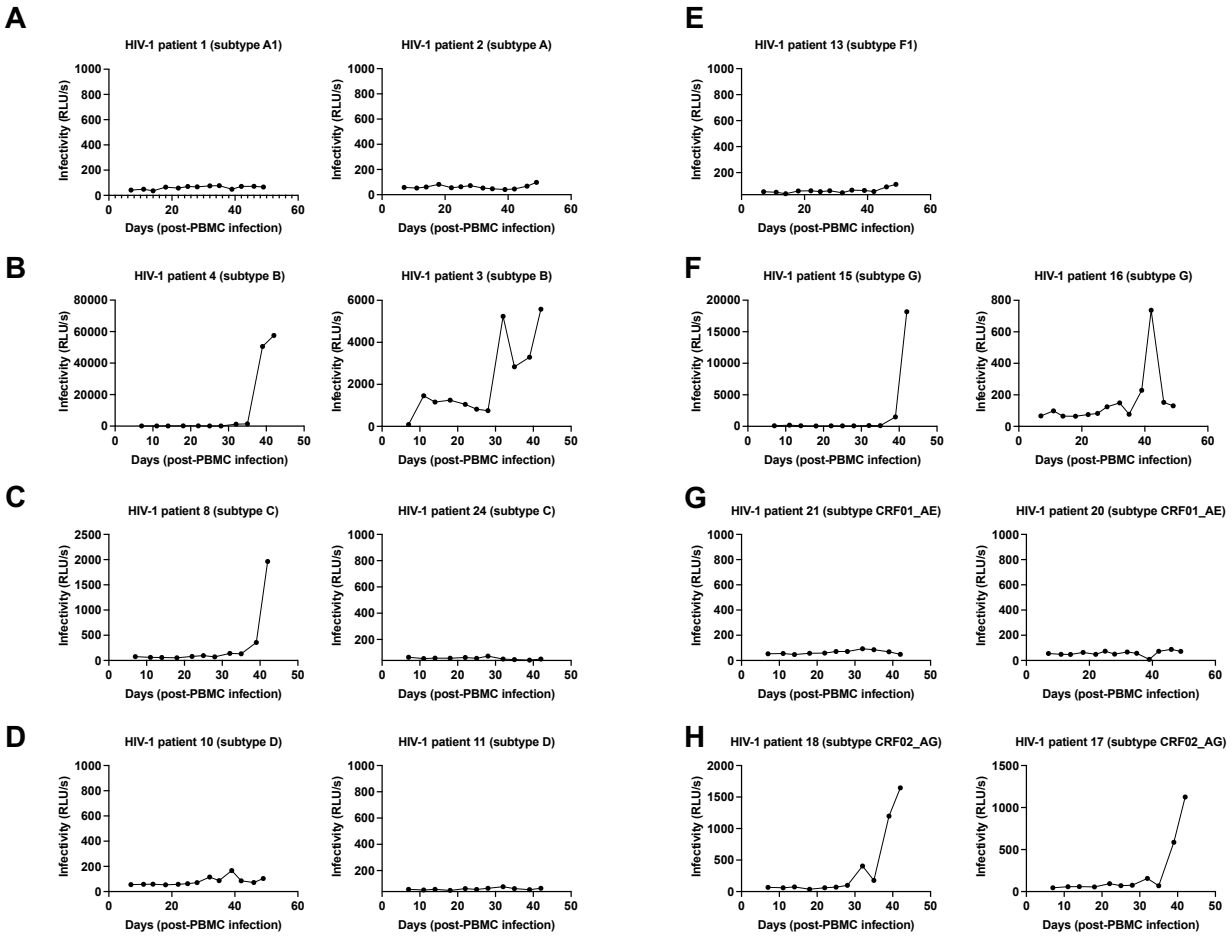
84-HPVHAGPIAPGQMREPR-100 **HIV-1**

84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

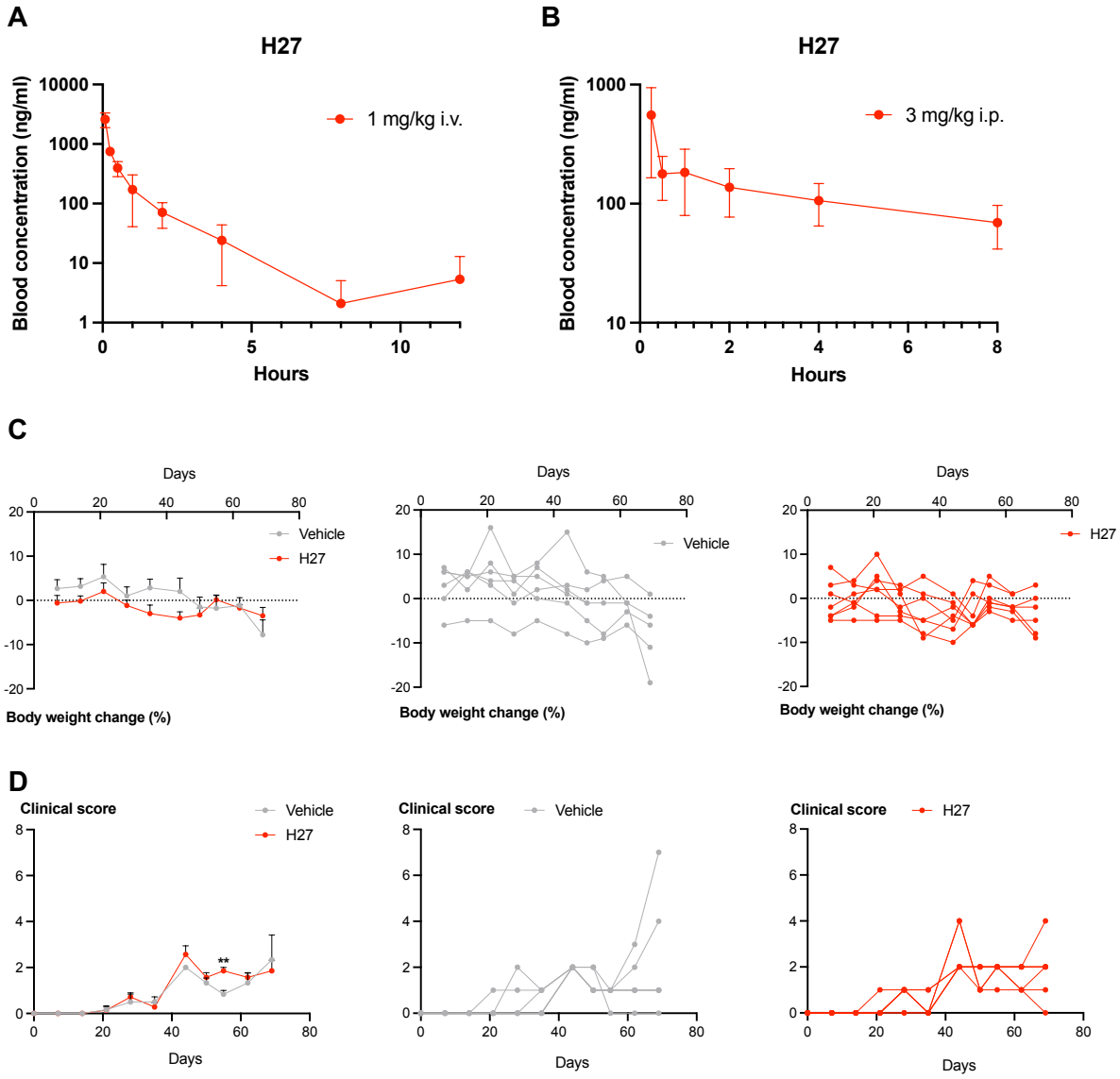
83-HPQPA–PQ–QGQLREPS-97 **SIVmac**

83 84 85 86 87 88 89 90 91 92 93 94 95 96 97

**Appendix Figure S10: Titration on HeLa-R5 cells of PBMC supernatants infected with patient plasma.** Infectivity was assessed on HeLa-R5 cells at 48 hpi using undiluted supernatants isolated at the indicated days after PBMC inoculation. β-galactosidase activity is provided as relative light units (RLU) per s. Infectious virus was successfully isolated from the plasma of 7 out of 15 patients. The first supernatant samples yielding an infectivity that was above 1000 RLU/s were selected for experiments shown in **Fig. 6A** to avoid the selection of mutations at later time points. The HIV-1 subtypes were **(A)** Subtype A, **(B)** Subtype B, **(C)** Subtype C, **(D)** Subtype D, **(E)** Subtype F, **(F)** Subtype G, **(G)** Circulating Recombinant Form CRF01_AE and **(H)** CRF02_AG.



**Appendix Figure S11: *In vivo* evaluation of H27 pharmacokinetics and toxicity. (A, B)** Pharmacokinetic evaluation of H27 in whole blood after single administration. Male C57BL/6 mice were injected **(A)** intravenously (i.v.) or **(B)** intraperitoneally (i.p.) with H27 at 1 or 3 mg/kg, respectively, with 3 mice per group. Serial blood sampling in the tail was performed at 5, 15, 30 min, then 1, 2, 4, 8 and 12 hours for each mouse following i.v. injection or 15, 30 min, then 1, 2, 4, 8 h following i.p. injection. The $t_{1/2}$ of H27 was 1.6 h after i.v. injection and 5.3 h by i.p. route. Results show the mean values from n = 3 animals at each time point ± SD. **(C, D)** Body weight and clinical scores following administration of H27. Female humanized mice were treated every 3-4 days from D37 to D44 and every 2 days from D48 to D69 with the vehicle (30% Kolliphor/ 70% H2O) or with H27 treatment at 3 mg/kg by intraperitoneal injection. **(C)** Body weight change from D7 to D69. Body weight change is calculated in reference to the body weight measured at D0. (Left) Average body weight change expressed as mean + SEM in % from D7 to D69. A two-way repeated measures ANOVA with Geisser-Greenhouse and Sidak's multiple comparisons tests was used. No statistical difference was observed. (Centre) Individual body weight change of the 6 vehicle treated mice from D7 to D69. (Right) Individual body weight change of the 6 H27 treated mice from D7 to D69. **(D)** Clinical Scores from D7 to D69. (Left) Average clinical score is expressed as mean + SEM from D0 to D69. A two-way repeated measures ANOVA with Geisser– Greenhouse and Sidak's multiple comparisons tests was used. ** p = 0.0088. (Centre) Individual clinical score of the 6 vehicle treated mice from D0 to D69. (Right) Individual clinical score of the 6 H27 treated mice from D0 to D69.


A
H27
Blood concentration (ng/ml)
10000
1000
100
10
1
0
5
10
Hours
1 mg/kg i.v.
B
H27
Blood concentration (ng/ml)
1000
100
10
0
2
4
6
8
Hours
3 mg/kg i.p.
C
Days
Vehicle
H27
Body weight change (%)
Days
Vehicle
Body weight change (%)
Days
H27
Body weight change (%)
D
Clinical score
Vehicle
H27
**
Days
Clinical score
Vehicle
Days
Clinical score
H27
Days

**Appendix Table S1: Exact p values for all figures.**

| Fig. 2G | | |
|---|---|---|
| Ordinary one-way ANOVA | Exact p value | Summary |
| H27 | 0.3369 | ns |
| PF74 | 0.0002 | *** |
| LEN | <0.0001 | **** |

| Fig. 5D | | |
|---|---|---|
| **CA::TRN-1** | | |
| Kruskal-Wallis test | Adjusted p value | Summary |
| DMSO vs. ni | 0.0016 | ** |
| DMSO vs. H27 | 0.0322 | * |
| DMSO vs. PF74 | 0.5406 | ns |
| DMSO vs. LEN | >0.9999 | ns |
| **CA::CPSF6** | | |
| Kruskal-Wallis test | Adjusted p value | Summary |
| DMSO vs. ni | 0.0004 | *** |
| DMSO vs. H27 | >0.9999 | ns |
| DMSO vs. PF74 | >0.9999 | ns |
| DMSO vs. LEN | 0.0155 | * |

| Fig. 6A | | |
|---|---|---|
| **YU2** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | <0.0001 | **** |
| DMSO vs. 10 μM | <0.0001 | **** |
| DMSO vs. 50 μM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 3** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | <0.0001 | **** |
| DMSO vs. 10 μM | <0.0001 | **** |
| DMSO vs. 50 μM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 4** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0160 | * |
| DMSO vs. 10 μM | 0.0007 | *** |
| DMSO vs. 50 μM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 8** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.2085 | ns |
| DMSO vs. 10 μM | 0.0086 | ** |
| DMSO vs. 50 μM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 10** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0223 | * |
| DMSO vs. 10 μM | <0.0001 | **** |

| | | |
|---|---|---|
| DMSO vs. 50 µM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 15** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | <0.0001 | **** |
| DMSO vs. 10 µM | <0.0001 | **** |
| DMSO vs. 50 µM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 17** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | 0.0001 | *** |
| DMSO vs. 10 µM | <0.0001 | **** |
| DMSO vs. 50 µM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| **Patient 18** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | <0.0001 | **** |
| DMSO vs. 10 µM | <0.0001 | **** |
| DMSO vs. 50 µM | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |

| Fig. 6B | | |
|---|---|---|
| **NL4-3** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0994 | ns |
| DMSO vs. 10 μM | <0.0001 | **** |
| DMSO vs. 50 μM | <0.0001 | **** |
| DMSO vs. 3TC | <0.0001 | **** |
| DMSO vs. NVP | <0.0001 | **** |
| **NL4-3 R263K** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0095 | ** |
| DMSO vs. 10 μM | 0.0007 | *** |
| DMSO vs. 50 μM | 0.0002 | *** |
| DMSO vs. DTG | 0.1888 | ns |
| DMSO vs. NVP | 0.0002 | *** |
| **NL4-3 G140S-Q148H** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0030 | ** |
| DMSO vs. 10 μM | 0.0003 | *** |
| DMSO vs. 50 μM | 0.0002 | *** |
| DMSO vs. RAL | 0.4917 | ns |
| DMSO vs. NVP | 0.0001 | *** |
| **NL4-3 N155H-K211R-E212T** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.0010 | *** |
| DMSO vs. 10 μM | 0.0002 | *** |
| DMSO vs. 50 μM | 0.0001 | *** |
| DMSO vs. RAL | 0.9893 | ns |
| DMSO vs. NVP | 0.0001 | *** |
| **NL4-3 I50V** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 μM | 0.3743 | ns |
| DMSO vs. 10 μM | 0.0133 | * |

| | | |
|---|---|---|
| DMSO vs. 50 µM | 0.0013 | ** |
| DMSO vs. DRV | 0.9266 | ns |
| DMSO vs. NVP | 0.0016 | ** |
| **NL4-3 V32I-L33F-I47V** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | 0.0003 | *** |
| DMSO vs. 10 µM | <0.0001 | **** |
| DMSO vs. 50 µM | 0.0001 | *** |
| DMSO vs. DRV | 0.3642 | ns |
| DMSO vs. NVP | 0.0001 | *** |
| **NL4-3 V106M** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | 0.0414 | * |
| DMSO vs. 10 µM | 0.0072 | ** |
| DMSO vs. 50 µM | 0.0008 | *** |
| DMSO vs. NVP | 0.9028 | ns |
| DMSO vs. 3TC | 0.0058 | ** |
| **NL4-3 M184V** | | |
| RM one-way ANOVA | Adjusted P value | Summary |
| DMSO vs. 5 µM | 0.0011 | ** |
| DMSO vs. 10 µM | 0.0009 | *** |
| DMSO vs. 50 µM | 0.0007 | *** |
| DMSO vs. 3TC | 0.1074 | ns |
| DMSO vs. NVP | 0.0009 | *** |

| Fig. EV2A | | |
|---|---|---|
| Wilcoxon test | Exact p value | Summary |
| Input 2h | 0.7500 | ns |
| Cores 2h | 0.2500 | ns |
| Friedman test | Exact p value | Summary |
| Input 16h | 0.9444 | ns |
| Cores 16h | 0.0046 | ** |

| Fig. EV2B | | |
|---|---|---|
| Ordinary one-way ANOVA | Adjusted P Value | Summary |
| DMSO vs. H27 | 0.0028 | ** |
| DMSO vs. 31 | 0.9415 | ns |