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online data

SUPPLEMENTARY ONLINE DATA

Inhibition of histone binding by supramolecular hosts

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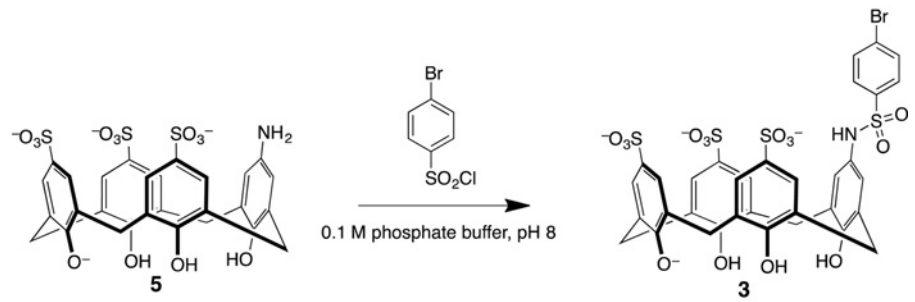
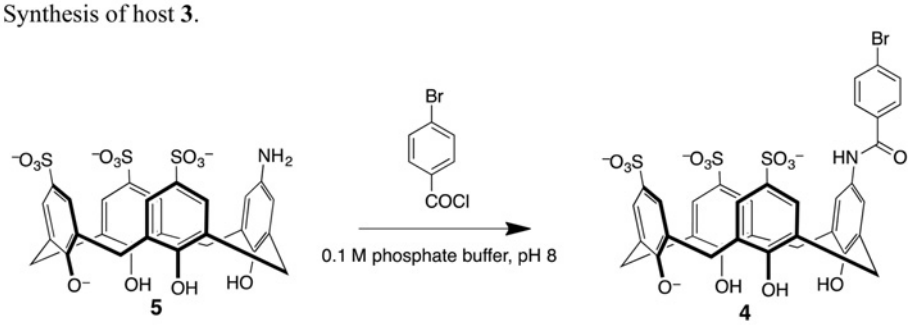


Synthesis of host **3**.



Synthesis of host **4**.

Figure S1 Synthesis of 3 and 4

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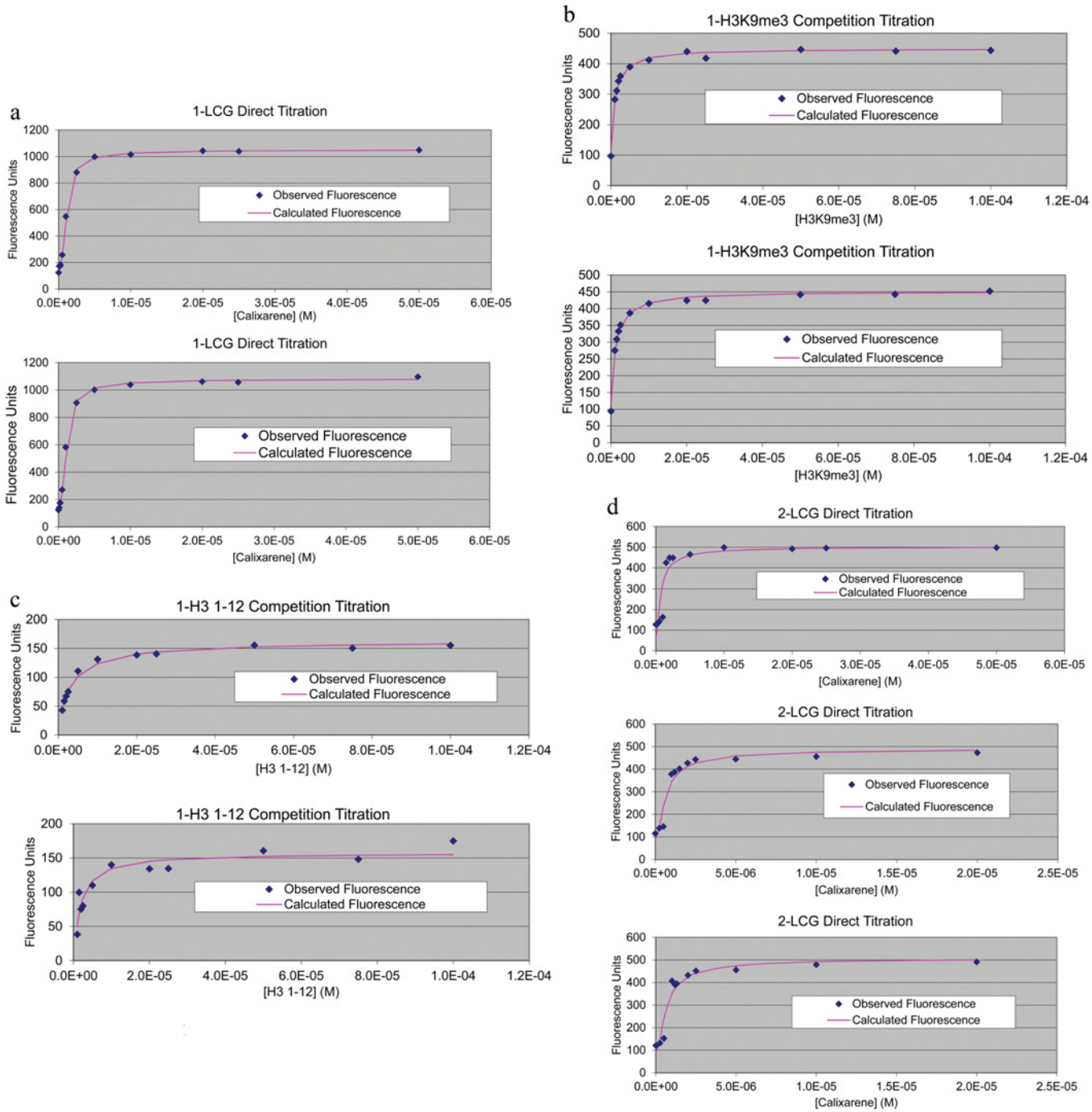

Figure S2 Direct binding and competition titration assays

See below for legend.

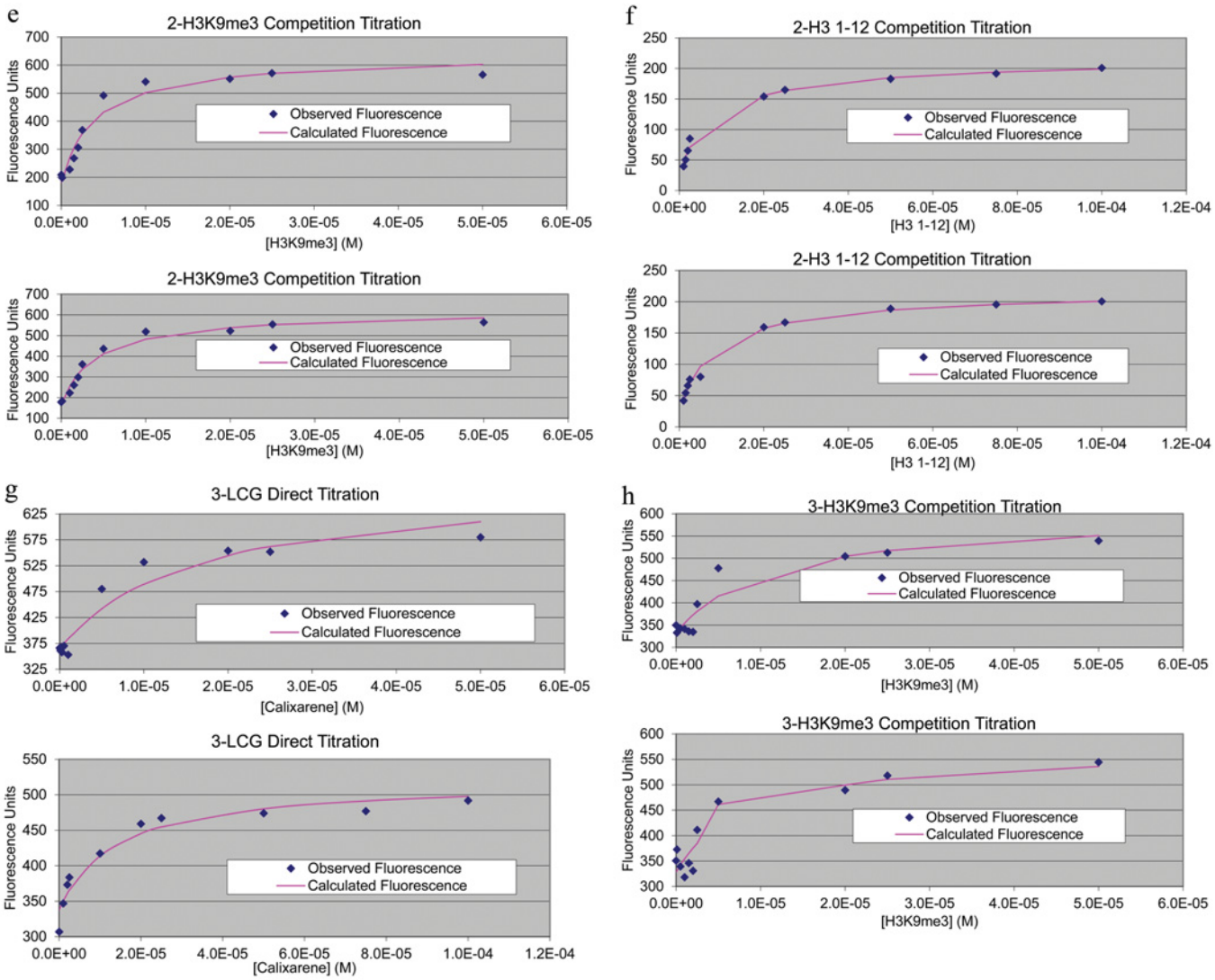

Figure S2 Continued

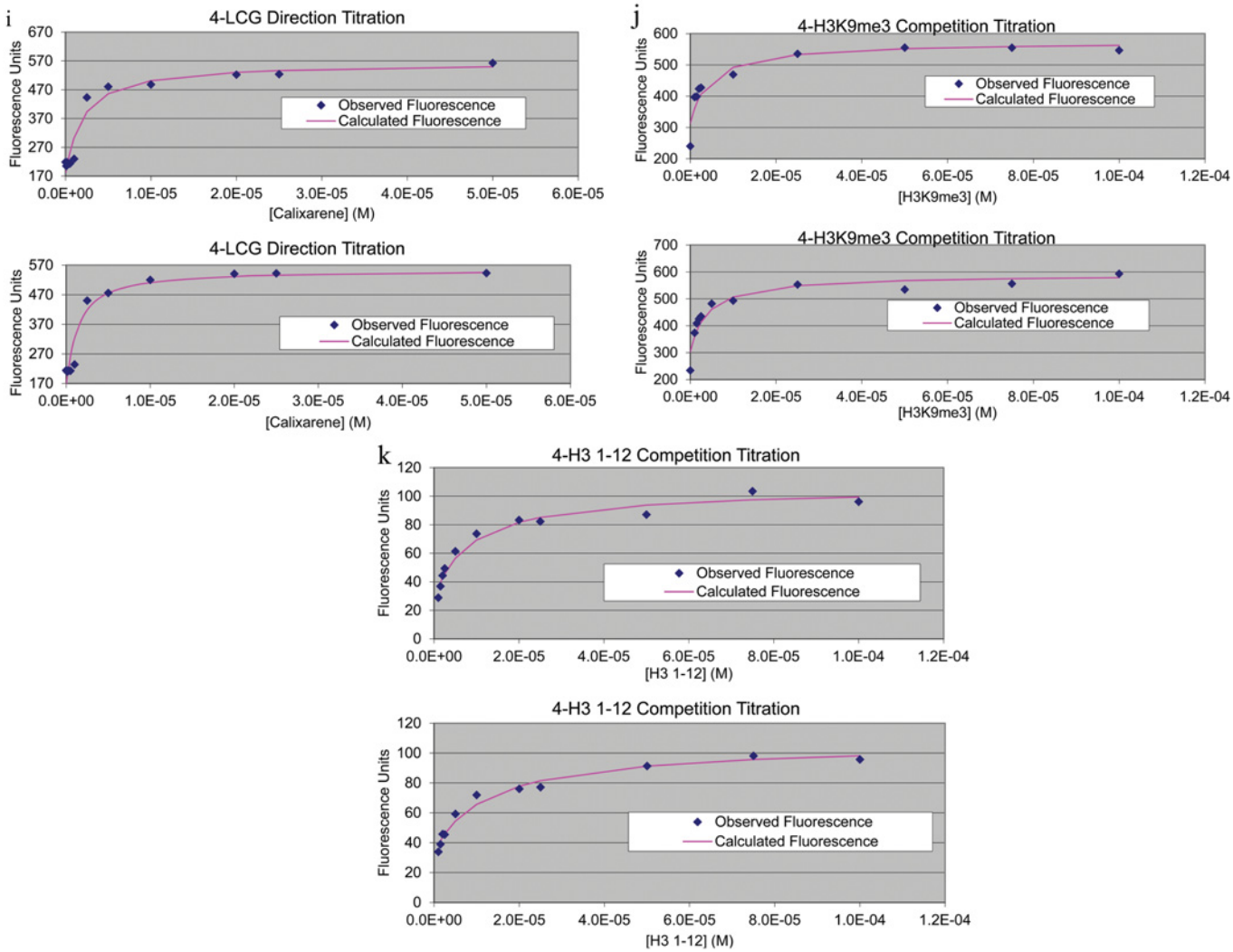

Figure S2 Continued

(**a**) Direct binding titration between **1** and LCG. (**b**) Competition titration between **1** and H3K9me3 peptide. (**c**) Competition titration between **1** and histone H3 1–12 peptide. (**d**) Direct binding titration between **2** and LCG. (**e**) Competition titration between **2** and H3K9me3 peptide. (**f**) Competition titration between **2** and histone H3 1–12 peptide. (**g**) Direct binding titration between **3** and LCG. (**h**) Competition titration between **3** and H3K9me3 peptide. (**i**) Direct binding titration between **4** and LCG. (**j**) Competition titration between **4** and H3K9me3 peptide. (**k**) Competition titration between **4** and histone H3 1–12 peptide.

Table S1 Binding constants, errors and r^2 values determined by fluorescence-based titrations and the program Equilibria

Averaged values determined by two to three replication titrations.

Compound	K_{ind} LCG $\pm$ S.D. (M^{-1})	r^2	K_{assoc} H3K9me3 $\pm$ S.D. (M^{-1})	r^2	K_{assoc} H3K9me0 (1–12) $\pm$ S.D. (M^{-1})	r^2
1	$(14.6 \pm 0.673) \times 10^6$	0.998	$(8.61 \pm 1.00) \times 10^6$	0.989	$(4.03 \pm 2.37) \times 10^6$	0.931
2	$(48.8 \pm 6.142) \times 10^6$	0.973	$(5.28 \pm 0.70) \times 10^6$	0.965	$(2.54 \pm 0.34) \times 10^6$	0.991
3	$(1.46 \pm 0.066) \times 10^6$	0.997	$(0.21 \pm 0.05) \times 10^6$	0.899	$<0.1 \times 10^6$*	–*
4	$(6.82 \pm 0.203) \times 10^6$	0.992	$(1.10 \pm 0.10) \times 10^6$	0.903	$(0.43 \pm 0.12) \times 10^6$	0.971

*Unable to fit weak binding at the concentrations used in the present study.

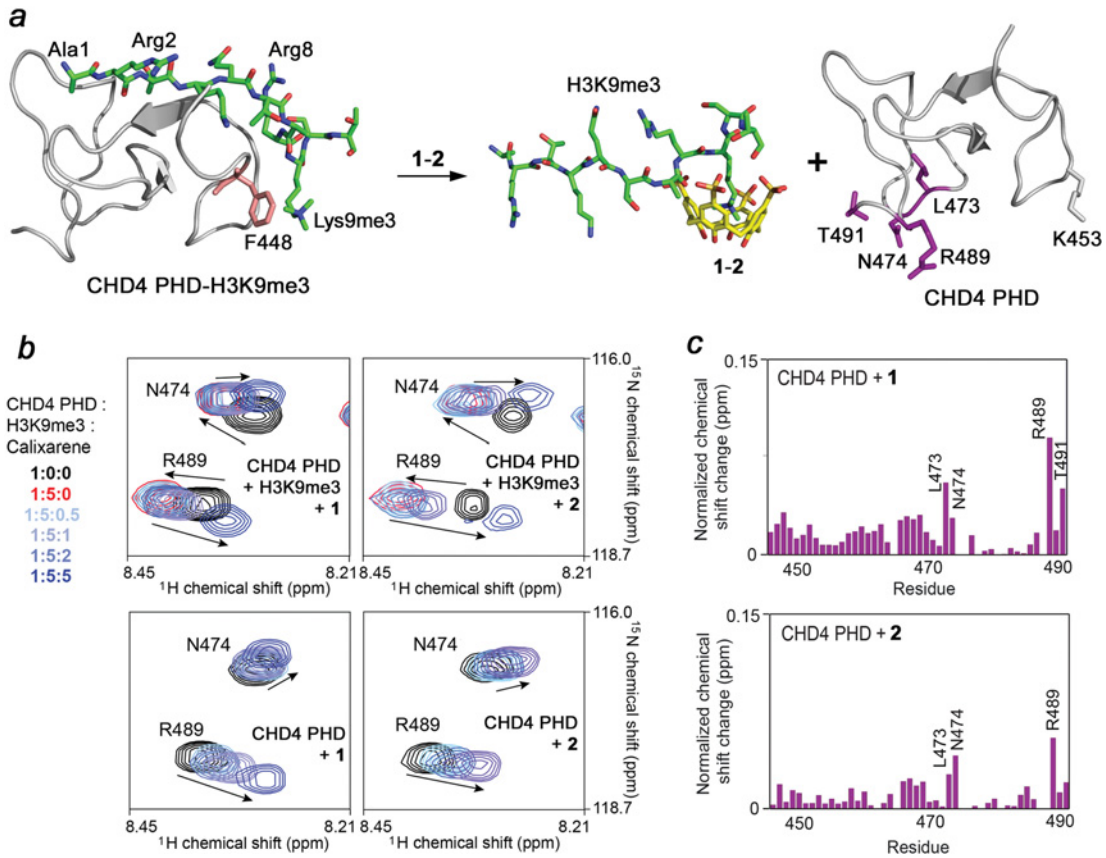

Figure S3 Calixarenes bind weakly to CHD4 PHD2 in the absence of histone peptides

(**a**) A model for the disruption of the CHD4 PHD2–H3K9me3 complex by calixarenes. The NMR structure of the complex (PDB code 2L75) with the protein (grey ribbon) and the peptide (green sticks) is shown. Residues of the PHD2 finger that are significantly perturbed upon binding of **1** and **2** are coloured purple and labelled. (**b**) Superimposed $^{1}H,^{15}N$ HSQC spectra of 0.15 mM CHD4 PHD2 collected as **1** or **2** were titrated, either in the presence of H3K9me3 (upper panels) or the absence of H3K9me3 (lower panels). Spectra are colour-coded according to the protein/peptide/calixarene molar ratio. (**c**) The normalized chemical shift changes observed in the CHD4 PHD2 finger upon binding of **1** or **2** as a function of residue.

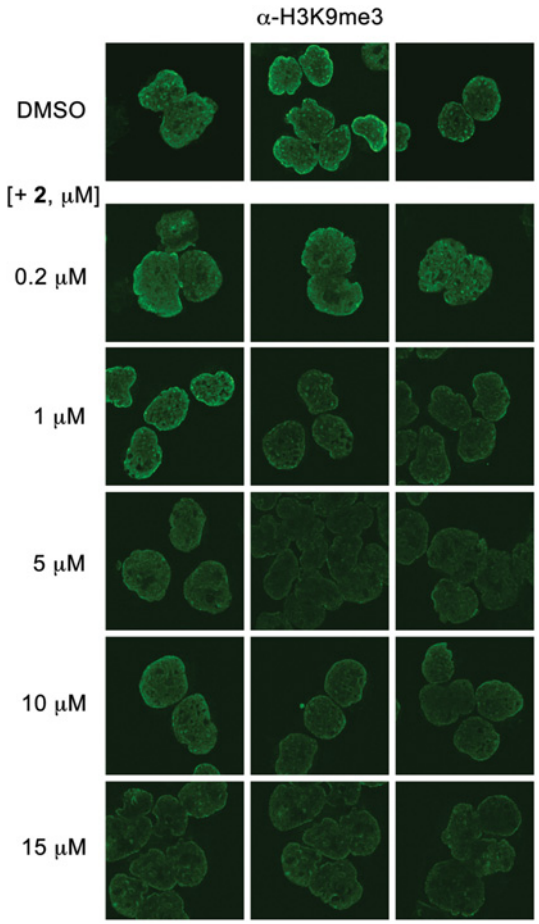

Figure S4 Representative images of immunofluorescence performed in HEK-293T cells upon the treatment with 1% DMSO only or in the presence of the indicated concentrations of 2

Cells were spotted on to slides and stained using an anti-H3K9me3 antibody.

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