



**Supplementary information, Fig. S1. MeCP2 drives chromatin compaction and chromatin liquid-liquid phase separation with DNA in vitro.**

**a** SDS-PAGE analysis of purified full-length MeCP2 and its related domain truncations.

**b** Top panel, in vitro phase separation assays for MeCP2 protein or 4X177-601 DNA (4xDNA) alone. Bottom panel, puncta formed by MeCP2 protein with 4xDNA in vitro. Scale bars, 20  $\mu\text{m}$ .

**c** Phase diagram of MeCP2 with PEG8000. Scale bar, 20  $\mu\text{m}$ .

**d** Top panel, FRAP recovery of MeCP2 with 10% PEG8000. Bottom panel, FRAP recovery of MeCP2 with 10% PEG8000. Scale bars, 20  $\mu\text{m}$ .

**e** FRAP recovery of MeCP2 with 4x601 DNA. Scale bars, 20  $\mu\text{m}$ .

**f** Time-lapse FRAP of MeCP2 with 4x601 DNA. Scale bars, 5  $\mu\text{m}$ .

**g** FRAP recovery of MeCP2 with 4x601 DNA. Scale bars, 2  $\mu\text{m}$ .

**h** FRAP recovery of MeCP2 with Mono-N. Scale bars, 20  $\mu\text{m}$ .

**i** 3D bar charts of %Area Occupied vs MeCP2 and Mono-N concentrations. Left chart: %Area Occupied vs MeCP2 ( $\mu\text{M}$ ) and Mono-N (nM). Right chart: %Area Occupied vs MeCP2 ( $\mu\text{M}$ ) and 4x601 NA (nM).

**j** FRAP recovery of MeCP2 with Mono-N. Scale bars, 2.5  $\mu\text{m}$ .

panel, snapshots of a punctum formed by MeCP2 and PEG8000 in Supplementary information, Fig. S1e during FRAP analysis. Scale bar, 2  $\mu\text{m}$ . Bottom, average fluorescence recovery traces of MeCP2 in puncta ( $n=6$ ). All data are presented as mean  $\pm$  SD. **e** Phase diagram of MeCP2 with 4xDNA. Scale bar, 20  $\mu\text{m}$ . **f** Fusion of droplets formed by MeCP2 with 4xDNA in S1e upon contact. Scale bar, 5  $\mu\text{m}$ . **g** Top panel, snapshots of a punctum formed by MeCP2 and 4xDNA in Supplementary information, Fig. S1e during FRAP analysis. Scale bar, 2  $\mu\text{m}$ . Bottom, average fluorescence recovery traces of MeCP2 in puncta ( $n=6$ ). All data are presented as mean  $\pm$  SD. **h** Phase diagram of MeCP2 with mono-nucleosomes (Mono-N). Scale bar, 20  $\mu\text{m}$ . **i** 3D phase diagrams of MeCP2 with Mono-N or 4xNA in Fig. 1g and Supplementary information, Fig. S1h. **j** Top two panels, snapshots of puncta formed in Fig.1g and Supplementary information, Fig. S1h during FRAP experiments. Scale bars, 2.5  $\mu\text{m}$ . Bottom, average fluorescence recovery traces of MeCP2 in puncta ( $n=6$ ). All data are presented as mean  $\pm$  SD.